

SAJOUS'S
ANALYTIC CYCLOPEDIA
OF
PRACTICAL MEDICINE

BY
CHARLES E. de M. SAJOUS, M.D., LL.D., Sc.D.
AND
LOUIS T. de M. SAJOUS, B.S., M.D.

WITH THE ACTIVE CO-OPERATION OF OVER
ONE HUNDRED ASSOCIATE EDITORS

TENTH REVISED EDITION

Illustrated with Full-page Half-tone and Color Plates
and Appropriate Cuts in the Text

VOLUME SIX



PHILADELPHIA
F. A. DAVIS COMPANY, PUBLISHERS

1922

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SAJOUS'S

ANALYTIC CYCLOPEDIA

of PRACTICAL MEDICINE

I

IODINE AND IODIDES.—

Iodine (*iodum*) is a solid, non-metallic element obtained from the ashes of seaweeds as well as from crude Chilean saltpeter. It was discovered by Courtois, a Parisian soda manufacturer, in 1812, and was first used in medicine by Coindet, of Geneva, in 1819. Though occurring most abundantly in deep-water seaweeds, iodine may also be detected in certain fresh-water plants, such as the water hemlock and water cress, as well as in the oyster, codliver oil, eggs and certain mineral springs. A common mode of preparation of iodine is to place the ashes of burned seaweed (kelp) in water, thus dissolving out the soluble salts, to remove chlorides and carbonates by evaporation and crystallization, to treat the residual mother-liquor with manganese dioxide and a mineral acid, and heating the mixture, when iodine can be distilled off.

Iodine occurs in friable, scaly crystals, bluish-black in color, having a metallic luster, and of a hot, acrid taste. It is soluble only in about 3000 parts of pure water, but dissolves readily in water containing salts, potassium iodide in particular. It dissolves in 10 parts of alcohol at ordinary temperatures, in

100 parts of glycerin, and is freely soluble in chloroform, ether, carbon disulphide, and glacial acetic acid. It volatilizes slowly upon continued exposure to the air, but, when heated, fuses at 114° C. and is dissipated in beautiful violet vapors at 180° C.

Iodine imparts a dark-yellow or brown color to all organic substances over which it is applied, except starch and all tissues containing it, which it colors blue owing to the formation of starch iodide. The blue coloration of this compound is so pronounced that it is made to serve as the basis of various tests for iodine. It is thus possible to detect this element in 450,000 times its weight of water. To ascertain the presence of iodine (in the form of iodides) in urine, fuming nitric acid is added to the latter. Iodine, if present, is thereby set free, and is usually recognized by shaking the mixture with chloroform, into which the iodine dissolves readily, imparting a characteristic purplish color. Previous partial evaporation of the urine facilitates the detection of iodine in it. Where an ammoniacal urine is being tested, Gillet advises that potassium hydroxide be added to it, in-order that the color of the iodine may not be

Collodium iodi, N. F. IV (iodine collodion), consisting of flexible collodion to which has been added 5 per cent. of iodine. Employed locally to produce the action of iodine.

Liquor hydrargyri et potassii iodidi, N. F. IV (solution of potassio-mercuric iodide; Channing's solution), made up as follows: Mercury biiiodide, 15 grains (1 Gm.); potassium iodide, 12 grains (0.8 Gm.); distilled water, 3 ounces (100 c.c.). Dose, 3 minims (0.2 c.c.).

Among the more important unofficial preparations of iodine are:—

Iodipin (iodized sesame oil), a yellow, oily fluid, tasting only of oil, and being essentially an addition product of iodine with the oil. It is prepared by the action of iodine chloride on sesame oil, and is supplied in two forms containing, respectively, 10 and 25 per cent. of iodine. Its action is that of the iodides, but is less sudden in advent and more prolonged. Dose, hypodermically, $\frac{1}{2}$ to $1\frac{1}{2}$ fluidrams (2 to 6 c.c.) of the 25 per cent. preparation; internally, 1 to 2 fluidrams (4 to 8 c.c.) of the 10 per cent. preparation.

Lipiodol, a clear, amber, neutral oily fluid, is described by Forestier as a chemical compound of 40 per cent. metallic iodine with oil of poppy seeds. The oil and iodine are so closely combined that the starch test fails to reveal free iodine. The expression "iodized oil," which has been applied to lipiodol, is in reality a broader term, including preparations made with other oils, such as iodipin.

Iodalbin, a reddish powder, with but little taste, and possessing a peculiar, sweetish odor. It is a compound of iodine and blood-albumin, and contains about 21.5 per cent. of

iodine. It is practically insoluble in the ordinary solvents, but dissolves slowly in alkaline solutions. Iodine fumes are evolved when it is heated. When ingested it passes practically unchanged through the stomach, but dissolves in the alkaline intestinal juices and acts in a manner similar to the soluble iodides. Dose, 5 to 10 grains (0.3 to 0.6 Gm.).

Iothion, a heavy, yellowish, oily fluid, chemically di-iodohydroxypropane [$\text{CHI}_2\text{I} \cdot \text{CIIOH} \cdot \text{CH}_2\text{I}$], and containing 77 per cent. of iodine. Its odor is peculiar but not unpleasant, and though insoluble in water, it dissolves in oils, glycerin, alcohol, etc. It volatilizes at the temperature of the body and is decomposed even by weak alkalis. Acting like iodine and iodides, iothion is used externally, being applied in the form of a 25 to 50 per cent. ointment, made up with equal parts of petrolatum and lanolin. It is said to undergo prompt absorption through the skin.

Sajodin, a colorless, odorless, tasteless and insoluble powder, chemically calcium monoiodobenenate [$(\text{C}_{21}\text{H}_{42}\text{ICOO})_2\text{Ca}$], and which should contain 26 per cent. of iodine and 4.1 per cent. of calcium. The compound becomes yellow superficially upon exposure to light, but this change is not accompanied by any important degree of decomposition. When heated, sajodin gives off vapors of iodine. It is used internally as a substitute for potassium iodide, over which it is said to have the advantage of relative freedom from untoward by-effects. Dose, 15 to 45 grains (1 to 3 Gm.) *per diem*; single dose, 8 grains (0.5 Gm.). See also the official *Calcii iodobenenas*.

Airol, aristol, and euophen have already been discussed under separate

headings, while iodoform will follow this article.

MODES OF ADMINISTRATION.—Potassium iodide is best prescribed in a grain-to-the-minim solution in water, of which the patient is required to take the prescribed number of drops in a half-glassful of milk as a vehicle. Sodium iodide is stated by Dock to have no decided advantage over the potassium salt in so far as taste and effect on the stomach are concerned, although certain observers have affirmed the contrary. The giving of large amounts of fluid with the iodides is one of the best means of avoiding iodism. Essence of pepsin (1 to 2 drams with each dose) is another vehicle that has been recommended for these salts, while Pfaff has advised the addition of 5 to 15 grains (0.3 to 1 Gm.) of sodium bicarbonate to each dose, in order to prevent free hydrochloric acid in the stomach from breaking the salt down to hydriodic acid. Huchard recommended combining with the iodide Fowler's solution, one drop to every 15 grains (1 Gm.) of iodide, up to 10 or 12 drops a day.

The compound syrup of sarsaparilla has been a favorite with many as a vehicle for iodides. Huhner, when continuing the same dose of iodide for a long time, prescribes:—

℞ *Potassii iodidi*. ʒj to ʒx (30 to 40 Gm.).
Syrupi sarsaparilla compositi fʒ (30 c.c.).
Aqua, q. s. ad fʒviij (240 c.c.).

M. Sig.: One teaspoonful in a half-glassful of milk or water three times daily after meals.

The same author warns that a pure preparation of the salt must be obtained, many bad effects being due to impurities. He also deems it best not

to prescribe a 100 per cent. solution of potassium iodide. It is possible to make up such a solution, but only with some difficulty. Most druggists would probably dispense a weaker solution. Where accurate dosage is of importance, it is safer to prescribe a 50 per cent. solution, 2 drops to equal 1 grain (0.065 Gm.) of the drug.

The dosage of potassium iodide is often to be made an ascending one. For this purpose, beginning, for example, at 10 drops of the grain-to-the-drop solution three times daily just after or a half or full hour after meals, the dose can be increased by 1 drop a day, or 1 drop every dose, etc. Often it is wise to discontinue the drug every three or four weeks for a few days, after which it is resumed at about half the amount at which it had been stopped, then increased as before.

Where sodium iodide is deemed preferable, a saturated solution may be used. The sodium salt is a little more soluble than that of potassium. The desired dose may be given in a glassful of water, $\frac{1}{2}$ hour after meals.

In a study of the elimination of iodine in the urine, the writers found that a maximum saturation of the tissues with iodine and the most durable action from it were obtained with iodized oil administered intramuscularly. Bonnamour and Delore (C. r. Soc. de biol., Dec. 27, 1924).

In children it is best to give the iodides very frequently in small doses— $\frac{1}{4}$ grain (0.015 Gm.) every hour. A convenient plan is to dissolve the daily dose in 24 teaspoonfuls of water and have the child take 1 spoonful every hour while awake and 2 or 3 spoonfuls on awakening after a two or three hours' sleep. In this way a six-month child may take as much as 15 or 30 grains (1 or 2 Gm.) in 24

hours for a long time without inconvenience (Huhner).

Iodine in organic combination (sajodin, etc.) remains a longer time in the system than potassium iodide, though less promptly absorbed. For mild forms of disease the organic preparations are suitable, but where a rapid action is desired, the inorganic are, in general, to be preferred.

The iodized proteins seem to be of advantage for therapeutic use only in so far as they avoid gastric irritation. The iodized fats and fatty acids seem to have some advantages when the continuous action of small amounts of iodine is desired. They are more slowly and evenly split. Their use in **arteriosclerosis**, **bronchial asthma**, **lead-poisoning**, etc., probably has some rational basis, therefore, on physiological grounds. The difference in frequency of iodism is probably due to the difference in the amount of available iodine present in the body at any one time. When large amounts of iodine are desired, as in **cerebrospinal syphilis**, avoiding the danger of iodism would be at the sacrifice of therapeutic efficiency. F. C. McLean (Archives of Intern. Med., Nov., 1912).

Where potassium iodide is not tolerated by stomach it may be administered by rectum, given in water, or, better, in milk, in doses of 15 to 30 grains (1 to 2 Gm.) three times a day. Its absorption is as rapid by this route as when it is given by the stomach, and may be even further accelerated by heating the solution to body temperature before its introduction. Potassium iodide can also be used hypodermically, pain being minimized if lukewarm water is employed. The subcutaneous use of iodipin is a valuable adjunct to treatment, notably in syphilitic disease of the nervous system and in chronic inflammatory conditions in general (Burnet).

To avoid gastric disturbance from iodine the writer sought an easily made compound in which it would be loosely combined with an organic substance. The formula for his preparation is:—

℞ *Iodine* 2.5 Gm. (38 gr.).
Tannic acid ... 4 Gm. (1 dr.).
Alcohol (90 per cent.) 38 c.c. (1¼ oz.).
Syrup, q. s. to make 75 c.c. (2½ oz.).

The iodine is dissolved in the alcohol. The tannic acid and 30 c.c. (1 ounce) of the syrup are then added. The solution is heated to just below the boiling point until it gives no evidence of iodine with the starch reaction. This requires about twenty minutes. It is then cooled, and the remainder of the syrup is added with flavoring. Each dram (4 c.c.) contains 2 grains (0.12 Gm.) of iodine. It may be given in doses of from ½ dram (2 c.c.) to 2 drams (8 c.c.) in water or wine before meals, according to age. The combination is especially well tolerated by children, and proved useful in cases of **chronic lymphadenitis**. It is indicated in children with **large faucial** and **pharyngeal tonsils**, in whom operation is contraindicated or objected to. V. H. W. Windgrave (Lancet, April 6, 1904).

To avoid irritating the gastric mucosa and to reduce to a minimum the phenomena of iodism, the author administers potassium iodide as follows:—

℞ *Potassium iodide*
 (chemically pure) gr. cl (10 Gm.).
Sodium bicarbonate (chemically pure) gr. cxx (8 Gm.).
Dry sodium phosphate 3j (4 Gm.).
Dry sodium sulphate ʒss (2 Gm.).
Boiled water Oij (1000 c.c.).
 M. Sig.: Dessertspoonful in water three times daily.
 Bourget (Théráp. des mal. respiratoires, 1911).

Intravenous administration of iodides or iodine has been more extensively resorted to of late. Frequently a 10 per cent. solution of sodium iodide is used, in doses of 5 to 10 c.c. (80 to 160 minims), given daily or every 2 or 3 days. Jeudwine, to induce hyperleukocytosis, has injected 1 to 2 c.c. (16 to 32 minims) of tincture of iodine (B. P.) diluted to 10 c.c. as a single dose, and likewise the same amount of a solution of 36 grains (2.3 Gm.) of potassium iodide in 1 ounce (30 c.c.) of water. These injections were given at intervals of 7 to 14 days.

Tissue reaction is more rapid when hypertonic sodium iodide solution is given intravenously instead of by mouth. In systemic *oidiomycosis* the writer used a 10 per cent. sodium iodide solution, boiled for 10 minutes, cooled, and given immediately by gravity, with 10 minutes elapsing during the introduction. Absence of ill-effects is attributed to the freshly made solution and the boiling. In *alopecia areata* and bone and periosteal lesions complicating syphilis, such intravenous iodide injections gave fairly quick results. F. J. Farnell (N. Y. Med. Jour., Sept. 5, 1923).

Pure iodine is used chiefly externally. In addition to the iodine tincture, compound solution and liniment, various solutions or ointments have been formulated for special purposes. Thus, Talbot, for purposes of oral disinfection, recommends the following "iodoglycerole":—

<i>R</i> Zinc iodide	3 parts.
Water	2 parts.
Iodine	5 parts.
Glycerin	10 parts.—M.

As compared with the ordinary tincture this preparation shows much greater astringency, while the glycerin causes rapid penetration, and irritation is minimized. The glycerin

also prevents the preparation from mixing with the saliva and running over the mouth. By frequent applications to the gum margins and teeth, the lips and cheeks being held away from the jaws until the iodine has dried, tooth decay can be arrested and oral disease greatly reduced. Before operative work in the mouth this solution can be used to disinfect the mucous membrane.

For use on mucous membranes, Stabler adds to equal parts of glycerin and water tincture of iodine, 1 dram (4 c.c.) to the ounce (30 c.c.), with a little belladonna and phenol as local sedatives. This solution is applied with a simple atomizer to the throat and nose, uterus, vagina, urethra, or skin. For the nose and throat, the patient holds the tube between the teeth with lips closed, and breathes through the nose, meanwhile working the bulb vigorously.

The following method of preparing "glycerole iodine" is recommended by T. W. Williams: Add 1 ounce (30 Gm.) of resublimed iodine to 12 ounces (360 c.c.) of alcohol, and sufficient potassium iodide to effect solution. Distill this over in a glass retort. To the product add sufficient C. P. glycerin to make 1 pint (480 c.c.). From this, iodine is readily absorbed through the skin or mucous membranes. In painful rheumatic or gouty joints the relief is almost instantaneous.

For external application with the intention of securing systemic absorption of iodine the following combination has been advised:—

<i>R</i> Iodine	3j (4 Gm.).
Spirit of ammonia ..	3j (30 c.c.).
Oleic acid	3ij (60 c.c.).
Liquid petrolatum ..	3iv (120 c.c.).

M.

If potassium iodide is incorporated with lanolin or resorbin and rubbed on the skin, no absorption occurs, but if 10 per cent. olive oil or petrolatum is added to the lanolin, iodine can be detected in the urine. Hirschfeld

and Pollio (*Archiv f. Derm. u. Syph.*, Nov., 1904).

If iodine be painted on the human skin in the dark, only a red light, such as that of an ordinary photographic lantern, being used, and the part immediately covered without exposure to white light, absorption will be rapid and there will be neither discoloration nor blistering, even after prolonged use. J. Dunbar-Brunton (*Brit. Med. Jour.*, Nov. 16, 1907).

Petrolatum and vasogen are good vehicles for potassium iodide to be absorbed through the skin, while wool-fat and lard give poor results. For iodoform petrolatum is also the best vehicle. Herzfeld and Elin (*Med. Klinik*, March 3, 1912).

Rapid absorption of iodine into the system can be secured by vaporization and inhalation. Thus Alter saturates a small amount of wool or absorbent cotton with tincture of iodine, ignites it and allows the patient to inhale the fumes as it burns. If this be done in a closed room, the air becomes charged with the vapors of iodine, and the latter will act more markedly than by ordinary methods of administration. The author has employed this method in catarrhal respiratory affections, tuberculosis, syphilis, etc. For the relief of dyspnea a little potassium chlorate may be added with advantage.

Minshall has had favorable results in affections of the nasal mucous membrane with a spray of iodine in purified liquid petrolatum.

For a description of the technique of "iodine fumigation" the reader is referred to the section on Therapeutics.

INCOMPATIBILITIES. — Iodine is incompatible with alkalies, alkaline earths, alkaloids, ferric salts, salts of mercury, tannic acid, oils and starch. With ammonia and oil of turpentine explosive compounds may be formed.

Tincture of iodine is incompatible with water.

The chief incompatibilities of potassium iodide are with the ordinary soluble metallic salts, with strychnine, hydrated chloral, tartaric acid, calomel, silver nitrate, potassium chlorate, alkaloidal salts, and with strong mineral acids.

CONTRAINDICATIONS.—In individuals known to have a marked idiosyncrasy to iodine, or in cases with organic disease of the kidneys or heart, the administration of preparations containing it, especially in large doses, is attended with some danger.

In pulmonary tuberculosis, or where there is merely a tendency to it, the administration of iodine or iodides is by many held to be unwise. Wells and Vetlesen observed the potassium salt to induce, or aggravate when already present, cough, expectoration, hyperemia, and râles in the affected or suspicious area in a large proportion of early cases of phthisis.

Yvert warns against placing yellow mercuric oxide ointment or calomel into the eye or mercury oxycyanide in the bladder of a patient who is taking iodine in any form. The iodine would act upon the mercury compound to produce mercurous iodide which, in the presence of an excess of iodine, would decompose into metallic mercury and the markedly caustic mercuric iodide, the latter causing aggravation of the local trouble. This mistake is most likely to occur in "strumous" children being given syrup of iron iodide internally and presenting also phlyctenulæ.

Acne rosacea and dermatitis herpetiformis are stated by Crocker to be aggravated by the use of iodides. In bullous eruptions he considers their use dangerous.

There is necessity for great caution with iodine in cases of arteriosclerosis with enlargement of the thyroid. Hyperthyroidism brought on by iodine does not cease when the iodine is suspended and it may progress to a serious form, as in several of the author's patients, who had taken but 1 Gm. (15 grains) of potassium iodide daily for two weeks. L. Krehl (Münch. med. Woch., Nov. 22, 1910).

To test for iodine in urine or saliva the writer stirs with the end of a match a little calomel into a few drops of the urine on a slide. If it contains iodine, the calomel turns bright yellow. Iodine in the saliva is shown up in the same way if the patient spits on a little calomel. This calomel test is extremely delicate and reliable. Another way to reveal the presence of iodine is by touching the tongue with a silver nitrate stick. The mark resulting is not white but yellow in case the individual has been taking iodine. Lesser (Berl. klin. Woch., Nov. 4, 1913).

In normal subjects potassium iodide, injected *intravenously*, is eliminated in a parallel manner in the urine and saliva. In cases of renal insufficiency it might *a priori* be supposed that an increase of elimination with the saliva would occur. As a matter of fact, the saliva eliminated no more iodide than the urine in these cases. The iodide seems to be fixed and retained by the tissues under these conditions. Ameuille and Sourdel (Presse méd., Apr. 24, 1919).

PHYSIOLOGICAL ACTION.

Externally.—When applied to the skin, iodine stains it a yellowish brown, owing to its actual penetration into the cells and combination with their protein constituents. Acting at first as a slight irritant, iodine causes, when repeatedly applied at short intervals, or when the preparation used is too concentrated, destructive changes which result in the shedding of the superficial cells and a

slowly developing reactive inflammation in the less seriously affected deeper structures. Its application induces a sensation of heat, together with burning or itching; there occurs dilatation of the superficial vessels, some edema and exudation of leucocytes, and in many instances vesicle formation. The more deeply lying vessels are believed to be, on the contrary, reflexly contracted, this probably accounting for the value of iodine as a counter-irritant.

Excessive irritation by iodine may cause pustules to form and deep inflammation to occur, with subsequent scarring. Iodine can be absorbed through the skin.

To remove iodine alcohol is the most effective agent, for it has itself a distinct bactericidal power. Hypo-sulphite of soda forms with iodine the soluble sodium iodide, which may be washed off with sterile water. This works best when the solution is quite warm, but it is not as effective as a solution of potassium iodide. This substance in a 10 per cent. solution can be thoroughly sterilized by boiling, and acts as a good solvent for the dried iodine. Later the surface is flushed off with sterile water. Hunter Robb (Surg., Gynec., and Obstet., Sept., 1913).

Upon mucous membranes iodine acts strongly but only superficially. Its tendency is to destroy tissues of low vitality and simultaneously excite healthy tissues to greater activity.

According to Lillie, potassium and sodium iodide are, next to the cyanides, the most active substances in increasing the permeability of cell walls, thus causing loss of the cell constituents, with ultimate cellular death. Zallard has shown that sodium iodide, applied over a large area of the skin in a 5 per cent solution, may be absorbed through

it, probably in sufficient amount to produce distinct therapeutic effects.

The destructive action of iodine on cell life is particularly pronounced in respect of micro-organisms. Kinnaman in 1905 showed iodine to be far superior to bichloride of mercury as a germicide. While the *Streptococcus pyogenes* was not destroyed by exposure for fifteen minutes to a 1:1000 solution of the mercury salt, a 1:500 solution of iodine killed the organism in two minutes. The *Staphylococcus pyogenes aureus* was killed by a 1:200 solution of iodine in five minutes, the *Bacillus tuberculosis* by a 1:100 solution in seven minutes, and the *B. anthracis* and *B. prodigiosus* by the last-mentioned solution in ten minutes. It is also superior to mercury bichloride in being stable when an iodide is included in its solution, in being non-toxic in effectual strength, in not coagulating albumin or forming inert compounds with tissues, and in possessing far greater penetrating power. The solution employed by Kinnaman in his tests was made up as follows:—

R Iodine 2.5 Gm. (38 gr.).
Sodium iodide 5.5 Gm. (80 gr.).
Sterilized water 250 c.c. (8 oz.).

M.

General Effects.—*Nervous System.*

—We have no definite knowledge of the direct effects of iodine on nervous structures, though the tremor, tonic or clonic convulsions, and altered reflex irritability noted after large doses would seem to indicate some excitant influence on nervous tissue on the part of such doses, and, as a matter of fact, accumulation of iodine in nerve-structures has been observed in cases of experimental intoxication in animals. Other phenomena, however, such as headache, prostration, vertigo, insomnia,

and mental confusion, are attributed by some to modifications in the blood-supply to the cerebral and medullary centers.

Circulation.—Reports upon the circulatory effects of iodine and iodides have been contradictory. Some authors have assumed a vasodilator action. According to Pouchet, moderate doses cause at first a fall in the blood-pressure, the power of the heart beats remaining, however, as before, and the rate being, if anything, slightly increased. (Hunt observed that the accelerator mechanism of the heart was less subject to fatigue after the administration of an iodide than before.) The reduction in pressure would suggest the existence of vascular dilatation, but Pouchet asserts that there occurs actually a vasoconstriction instead, and that the lowering of pressure is due in reality to a diminution in the total amount of fluid circulating in the vessels, the researches of Henrijean and Corin having shown the red-cell count to be enormously increased three hours after an iodide injection. The excess of fluid is asserted to pass out of the vessels not only through the kidneys, but by transudation into the serous cavities, into the lungs (pulmonary edema), and even, in certain cases, into the subcutaneous tissues. In a second phase of the circulatory effects of iodine, the blood-pressure rises again to above normal, and the heart rate, if previously accelerated, sinks to about the usual figure. This condition is due both to persisting vasoconstriction and to a return of fluid into the blood-vessels through the lymphatics, as is shown by a secondary fall in the number of red corpuscles per cubic millimeter, which at times betokens even a certain degree of hydemia.

These phenomena occur as well, it not quite as markedly, where sodium iodide is used as with the potassium salt, and hence are to be attributed directly to the iodine ion.

Toxic doses of iodine give rise, according to Pouchet, to the following series of circulatory changes: (1) immediate slight increase of heart rate; (2) slowing, with increased amplitude of heart beat, and constant blood-pressure; (3) diminished cardiac strength, with blood-pressure remaining, nonetheless, practically the same; (4) further cardiac weakening, with accelerated rate and a marked fall in blood-pressure. In general iodine diminishes the irritability of depressor and inhibitory nerve-structures, and, on the contrary, excites the sympathetic. It is especially or exclusively free iodine which acts directly on the circulation; minute amounts of the element added to fluid that is being perfused through a turtle's heart are sufficient to arrest its action, while much more concentrated solutions of sodium iodide are required to produce the same effect.

On the whole, valid experimental evidence that the iodine in iodides acts as a vasodilator is conspicuously lacking. Stockman and Charteris concluded from their clinical and experimental observations, moreover, that neither potassium nor sodium iodide when given to man by the stomach in ordinary doses, depresses the heart or lowers the arterial blood-pressure.

Lymphatic System.—Iodine is credited by Martinet and others with being a lymphagogue, this in turn being related to the transudation of fluid from the blood-vessels into the tissues which was referred to in the preceding section. The lymph, becoming more rich in salts than normally, owing to the addition

of those from the blood, extracts water from the surrounding tissues or pathological exudates. This extra fluid then re-enters the blood-stream, carrying with it waste material washed from the tissues, which material is soon eliminated through the emunctories. Where this process remains within certain limits, therapeutic effects are alone produced; where it proceeds too far, however, edema—even pulmonary edema—is the result.

Another effect of iodine having to do with the lymphatic system is that of markedly stimulating lymphoid tissue in general, as well as serous membranes, the result being a pronounced increase in the production of lymphocytes, especially where small doses are used and only for a short time (Lortat-Jacob). If excessive doses be given, or smaller ones for too long a time, sclerosis of the spleen and lymph-nodes may instead be induced (Pouchet).

Secretions.—Iodine and iodides tend to increase the flow of secretions from most glands, especially the salivary, buccal, nasal and lachrymal glands. Its elimination takes place in part through these channels. The sweat secretion is, however, not much affected by it, while the mammary secretion is diminished or even checked. The output of urine may be temporarily augmented.

Metabolism.—Iodine markedly enhances tissue change, as is shown by the increase in total urinary nitrogen which constantly follows its administration. The phosphates in the urine are likewise increased only temporarily, by alkaline iodides or organic compounds of iodine. The elimination of chlorides is greatly augmented, sometimes threefold,—an eloquent exemplification of the lymphagogue action of iodine. Proteins and fats with which iodine combines in the

system are thereby rendered more susceptible to decomposition. Hence the loss of body weight which the administration of iodine or iodides in sufficient dosage may produce, and the observation of Winternitz that animals could be fattened on iodized fats only if the proportion of iodine contained in the latter was kept below a certain small percentage (Pouchet). The respiratory quotient, *i.e.*, the ratio of oxygen taken in to carbon dioxide eliminated, is increased by iodine, this showing that compounds rich in oxygen are reduced to form compounds poor in oxygen and extra carbon dioxide. The resulting compounds can only be fats, and this harmonizes with the fact that in animals subjected for prolonged periods to large daily doses of iodides, fatty degeneration, especially of the liver and kidneys, may be observed.

Apparently the influence of iodine in causing tissue destruction is exerted particularly on the more simple or recently acquired forms of cells. Fibrous tissue is thus particularly susceptible to its destructive or softening effect, as exemplified in the use of potassium iodide in various sclerotic conditions.

A doubling, trebling, and even quadrupling of the *non-protein nitrogen of the blood* was noted after small doses of either potassium or sodium iodide. Grabfield (Jour. Amer. Med. Assoc., Aug. 19, 1922).

Determining the basal metabolism after ingestion of iodides, the writer found that large doses gave variable results in healthy subjects. In hypothyroid goiter patients the oxygen consumption increased to normal figures. The majority of the hyperthyroid patients responded to the iodine with a lowering of the metabolism; in some, however, the metabolism increased excessively. In such cases the iodine must be gradually reduced and discon-

tinued. Iodine treatment must be done under continuous control of the metabolic rates, especially in exophthalmic goiter. Liebesny (Wien. klin. Woch., May 22, 1924).

An increased rate of erythrocyte sedimentation found in 4 out of 5 patients who had been taking 0.5 Gm. (7½ grains) of potassium iodide 3 times a day for 14 days. The author attributes this result to a change of surface tension of the erythrocytes. Ephraim (Klin. Woch., July 29, 1924).

Study of the effect of sodium, lithium, calcium, potassium, strontium and magnesium iodides, Lugol's solution, and sajodin on the *nitrogen metabolism* of normal human subjects. It was found that the exhibition of any of these drugs increases the urinary nitrogen excretion of subjects in positive nitrogen balance on a constant protein intake. When sodium, lithium, strontium or magnesium iodides are exhibited the increase in nitrogen output is immediate. When calcium or potassium iodides are given it is delayed, occurring, in these experiments, after the 3-day period of drug administration. Changes in the non-protein nitrogen of the blood correspond to urinary changes, *i.e.*, falling if the rise in urinary output is immediate, and rising until the increased excretion begins when the latter is delayed. Grabfield and Prentiss (Jour. of Pharm. and Exp. Therap., June, 1925).

Absorption and Elimination.—

Iodine may be absorbed in small amount when applied to the skin. Taken internally, it is freely absorbed, but enters the blood as an iodide or in combination with proteins, as it readily enters into chemical unions of various sorts and cannot long exist free in contact with the tissues. The resulting iodine compounds are, however, themselves readily decomposed by various agencies, and it is considered likely that, at least for a time, the action of free iodine in small amount is exerted upon the economy. In view of the foregoing, it

will readily be seen that the effects of iodine and iodides must be to a great extent the same.

The average absorption of sodium iodide, quantitatively, is about the same for all divisions of the small intestine; from the stomach and colon it is about a third less. The absorption from the intestine was at first very rapid, from 50 to 75 per cent. being absorbed within ten minutes; then the absorption was greatly checked or completely arrested, so that from 25 to 50 per cent. might remain unabsorbed at the end of two hours. Visible hyperemia induced locally by various drugs increased, while visible anemia diminished the absorption of iodide. Injury of the intestinal epithelium, however produced, hindered the absorption. Feeding dogs on a chloride-poor diet, thus rendering the tissues in general poor in chlorides, did not appear materially to increase the absorption of sodium iodide. Hanzlik (*Jour. of Pharm. and Exper. Therap.*, March, 1912).

In a pharmacological study of the distribution of iodide compounds in normal animals, rabbits, guinea-pigs, and a few dogs and cats the iodide compounds, potassium iodide chiefly, iodopin, sajodin and iodine-albumin, were given subcutaneously and per os. The quantity of iodine in various organs and tissues was quantitatively determined.

1. When an iodine compound is absorbed, the iodine is usually found in largest quantities in the blood and wherever blood is present. Used therapeutically as potassium iodide, the iodine is found in fatty tissues, the brain and spinal cord, besides the blood. 2. The amount of iodine contained in 1 Gm. (15 grains) of any organ; the iodine content of each quantitatively is in the following order: blood, kidney, lung, liver, muscle, and brain. Other organs show various amounts under different conditions. The kind, mode of use or quantity of the iodine compound have

no marked influence on the distribution of the iodine. 3. Although a part of the iodine is fixed in the organs, one cannot tell whether it is secreted specially by any organ.

4. *a.* Iodine in blood serum and plasma occurs only as potassium iodide when this salt is used and cannot be found as organic compound. In coagula and the blood corpuscles, iodine occurs in organic combination with fat and lipoid, but not with proteid. *b.* When iodine-proteid is used, the iodine is found in the blood both in fat and lipoid, but also with proteid. *c.* When the iodine-fat is used, the iodine is found in the blood combined with fats and lipoids but not with proteids. *d.* The quantity of iodine combined with fat and lipoid is least when potassium iodide is given, greater when iodine proteid and greatest when iodine-fat is administered. Kamiji Fujisawa (*Sei-I-Kwai Med. Jour.*, Jan. 10, 1918).

Once absorbed, iodine or its compounds is taken up by the body cells, the amount present in various tissues depending upon the relative affinities of the latter for it. According to Labbé and others, iodine is taken up abundantly in the spleen and lymph-glands and next in the liver. Iodine is also stored, in still larger amount, in the thyroid gland, becoming a constituent of its thyroxin. The iodine content of the normal gland can be increased by giving iodine or its compounds. Up to a certain point the thyroid abstracts iodine from the blood with great rapidity. Marine and Rogoff, injecting 50 mgm. of potassium iodide intravenously in dogs, found that fixation in the thyroid was complete in 5 minutes, and that none of this dose of the drug was fixed by the liver or spleen.

Disease alters adaptability to retain iodine, so that tuberculous or carcinomatous tissue contains more iodine than the same tissue in health.

Secreting glands which are diseased by syphilis contain from three to six times as much as normal blood, and the less severe the syphilis, the greater the readiness of the tissue to hold iodine. In such tissues the iodine is in an organic combination. O. Loeb (*Arch. f. exp. Pathol.*, Bd. lxix, S. 108, 1912).

Under normal conditions the thyroid has the greatest affinity for iodine of any organ of the body; it can therefore store iodine electively when it is circulating in the body fluids even in very weak dilution. Iodine introduced in the body can be found in any tissue the seat of inflammatory change, and even in any portion of tissue that has become foreign to the body in any way. Diseased bone-marrow and spleen, except in leukemias, frequently show an abnormally high iodine content. Normal organs can fix iodine according to their internal secretory capacity; this is true, in particular, of the pituitary. Fixing of iodine in general makes the organ smaller. Goiters poor in iodine and which have lost their iodine-fixing capacity may have this elective property restored temporarily or permanently by iodine in proper dosage. The catabolic action of iodine on iodaffin tissue may be logically applied in the treatment of neoplasms. Iodine makes the red blood cells larger and richer in albumin and hemoglobin, and frequently gives them greater osmotic resisting power. G. Holler (*Klin. Woch.*, Sept. 3, 1923).

According to Pouchet, the leucocytes are especially charged with the task of distributing iodine in the system. Under the microscope, these cells can be observed to absorb iodine, showing for a time a reddish-yellow crescent at their periphery, after which the element is quickly changed to "masked" iodine, *i.e.*, iodine so combined that its ordinary chemical reactions can no longer be elicited. Contact of an iodine solution with a serous surface causes a prompt afflux

of leucocytes, which become agglutinated, and endothelial desquamation. The appearance of numerous large mononuclear leucocytes, as well as some macrophages or phagocytic cells, is a marked feature of the resulting situation, and suggests that iodine is a specific excitant of defensive leucocytic activity.

The elimination of both iodine and iodides occurs in the form of the latter, chiefly through the kidneys, and in less proportion with the saliva, respiratory passages, sweat and mammary secretion. Large doses of iodine tend to irritate the kidneys, as shown by the appearance of albuminuria and possibly, in rare instances, nephritis. Broeking has shown that the excretion of potassium iodide in the urine amounts to nearly 80 per cent. of the quantity ingested. The principal excretion takes place during the first few hours, and within the first twelve hours about 75 per cent. of the total excreted iodine is demonstrable in the urine; the remainder is eliminated, at least in the case of a single small dose, within sixty hours. Only traces appear in the feces. Rogovin found that iodine can be detected in the urine usually after 0.005 Gm. ($\frac{1}{12}$ grain) and sometimes even after only 0.002 to 0.003 Gm. ($\frac{1}{30}$ to $\frac{1}{20}$ grain) of potassium iodide has been given by mouth. According to Ménière, absorption of iodides takes place and elimination with the saliva begins on an average in from eight to ten minutes, though if the stomach is quite empty and the iodide is given in warm tea, this period may be shortened to two or three minutes; where the stomach is full, there is, on the other hand, a delay of thirty or forty minutes.

Fischel found iodine in the urine only in the second hour after administration of sajodin by mouth, showing that this organic combination of iodine is more slowly absorbed than the inorganic iodides.

Testing the excretion of strontium iodide in the human subject in comparison with that of sodium and potassium iodides, the writers found practically no difference in the rate of excretion of the 3 compounds. The excretion of strontium iodide not being slower, neither is its absorption to be considered slower, since all iodides are believed to exist in the blood and tissues essentially as sodium iodide. Krahulik and Pilcher (*Arch. of Int. Med.*, Jan., 1918).

In clinical tests, the writer found both sodium and potassium iodide practically entirely eliminated from the body by the end of 96 hours, regardless of the size of the dose. Absorption to the extent of 96 per cent. took place from the gastrointestinal tract, in spite of the fact that 20-Gm. (300-grain) doses were followed by a mild watery diarrhea. There is less gastric irritation if the drug is taken on an empty stomach, $\frac{1}{2}$ hour before meals. Sodium iodide is usually better tolerated than the potassium salt.

There was no striking difference in the rate of elimination of sodium iodide given intravenously as compared to oral administration. Practically all adult patients tolerate 100 c.c. ($3\frac{1}{2}$ ounces) of 10 per cent. sodium iodide solution intravenously, and no accumulation occurs even upon daily injection. A dose of 2 to 3 Gm. (30 to 45 grains) by mouth proved equivalent to the most efficient dose by rectum, *viz.*, 3 to 10 Gm. (45 to 150 grains) a day.

The potassium and sodium salts seemed to behave differently in absorption, the former forming a sodium protein combination, while in the case of the latter, only traces of iodine entered into combination with the proteins in the blood. In 2 patients with symptoms of iodism following sodium

iodide by the mouth, the iodine was found to have united with the protein fraction to a greater extent than in normal persons. E. D. Osborne (*Jour. Amer. Med. Assoc.*, Aug. 19, 1922).

UNTOWARD EFFECTS AND POISONING. IODISM.—The untoward effects most frequently met with from iodine or iodides are the earlier manifestations of chronic iodine poisoning or "iodism." Coryza and profuse discharge from the mucous membrane of the upper respiratory tract, ptyalism, and an acneiform eruption generally starting over the shoulder-blades constitute, in the majority of cases, the initial symptoms of this condition. There may also be noticed puffiness of the face, a peculiar metallic taste, particularly early in the morning, slight tenderness of the teeth and gums, lack of appetite for breakfast, frontal headache, lachrymation, and sore throat. These phenomena may appear after only a few doses have been taken in persons with a distinct unusual susceptibility to the drug, but in the majority of instances they do not occur until the dose administered has become quite large.

Because of a slight ailment indicating potassium iodide, the author took three doses of about 2 grains (0.13 Gm.) each in solution, at intervals of three or four hours. Before the second dose, the conjunctiva of his right eye began to inflame; after the second dose it became rapidly worse, and after the third dose it became so bad that he suspected the iodide as the cause, and so took no more. The inflammation persisted, in spite of treatment, for a week.

Some time after he took a dose of iodide in solution, unintentionally, not exceeding 4 grains (0.26 Gm.); five or six hours afterward the conjunctiva of the right eye became highly inflamed, exuding sticky mucus, and the upper and lower eye-

lids very edematous; this was accompanied by severe pain and heat in the eyeball. Vision was unaffected. He also became slightly hoarse, and had a slight aching in the larynx. Upon application of cold-water packs the trouble subsided in thirty-six hours. T. Julian (*Chicago Med. Times*, Oct., 1908).

A man aged 67 applied tincture of iodine on three successive days to painful areas following intercostal neuralgia, and covered it with oil-cloth. Some days later an eruption suddenly appeared, consisting of acne-like papules with small pustules upon the tops, surrounded by a red halo. This eruption spread over the whole body. Upon the limbs and the trunk there was also a macular eruption. There was no fever or other constitutional disturbance. There was some inclination to regard the eruption as either varioloid or varicella. Hodara (*Dermat. Woch.*, Nu. 10, 1912).

Sudden total blindness following the application of a 10 per cent. iodine solution over a severe tenosynovitis and a Colles fracture. In four days the patient developed a general edema of the arm and herpes of the arm and left side of the face, which also became edematous; after about four days this subsided. In four days after the subsidence of these symptoms she awoke in the night to attend to something for her children and found she could not see at all; she could not tell where the light was. Besides the blindness she had a complete paralysis of both upper lids.

While paralysis of the various oculomotor branches and of the levator palpebræ has been reported, no case of blindness is mentioned, though under the caption "Bromide Poisoning" there are such mentioned. The not infrequent occurrence of sudden death after fractures resulting from thrombosis suggest this as a possible cause for the blindness. E. J. Bernstein (*Ophthalmology*, Oct., 1913).

In severe cases there may be distinct nausea, diarrhea, marked headache, malaise and progressive emaciation and anemia. The skin eruption may assume various appearances, advancing from a simple acne or dermatitis to an exanthem simulating that of small-pox, varioloid, pemphigus, purpura, eczema, etc. Sometimes large boils appear. There may also develop parotitis, cardiac palpitation, sweating and fever.

A patient had been ordered a saturated solution of potassium iodide. On the fourth day he was taking three doses of 13 drops each. On this day his finger-tips showed slight cyanosis. The drug was discontinued for the entire fifth day and the local cyanosis disappeared within twenty-four hours.

On the sixth day, one single dose of 14 drops was given. During the night there appeared a diffuse ecchymosis under the entire skin of all the fingers and thumbs, stopping very abruptly at the metacarpophalangeal joints. The fingers, in addition, were numb, cold, stiff, slightly swollen, and very painful. The little finger of each hand was almost absolutely black. The extreme tip of the nose was similarly affected, though less severely. The toes remained entirely normal, but there were a few isolated, mild purpuric spots on the thighs and on one arm.

Under the assiduous application of warmth and friction, the condition very gradually subsided. It was nearly three days before the patient felt quite reassured that the fingers and nose were safe from gangrene. There had been no gastric irritation, coryza, acne, or any other symptom of iodism. Gathmann (*Med. Record*, Jan. 30, 1904).

A man, aged 52 years, presented an eruption of tumor-like and papillary elevations scattered over the scalp, face, trunk, and extremities after taking considerable doses of iodide of potassium. The eruption was accompanied by some elevation of

temperature and evidences of renal insufficiency. One of the most characteristic lesions, situated on the forehead over the left eye, was a quarter-dollar-sized, soft, rounded tumor with a broad, constricted base and ulcerating summit. A portion of this tumor examined microscopically showed a structure closely resembling epithelioma, there being the same connective-tissue *loculi* filled with atypical epithelial cells. D. W. Montgomery (Jour. of Cutan. Dis., Feb., 1904).

Case of tertiary syphilis in which the administration of three 10-grain (0.65 Gm.) doses of potassium iodide caused a variolous rash. Small-pox was present in the town, but it was excluded in this case for the following reasons: (1) absence of its prodromal symptoms; (2) mature, reticular nature of the eruption; and (3) hemorrhagic nature of the eruption, unaccompanied, at first, by grave illness of the patient. The diagnosis was confirmed by the appearance of bullæ and by the reappearance of the rash when iodide was readministered. Hynes (Lancet, Feb. 13, 1904).

Purpuric eruptions caused by the ingestion of the iodides may be divided into two provisional groups. The first group includes the extensive petechial and hemorrhagic bullous cases, which occur in those individuals with organic disease, particularly of the kidneys or the heart, or with a lowered condition of the general economy, making them more susceptible to the effect of the drug, or with a strong idiosyncrasy to the same. The second group includes all cases with a localized distribution, particularly those in which the eruption is limited to the lower extremities or the lower legs, which occur in individuals in perfect health, and are explainable only in that a mild idiosyncrasy to the iodide is present.

Mild symptoms of iodism were present in a few of the 61 cases collected by the author, and severe reaction to the drug was noted in 2 cases. Edema of the glottis was

found in 2 instances. Lesions were found on the mucous membranes in a few cases. Organic disease of the kidneys and heart were found in but 10 cases. The various salts of iodine are capable of causing a purpuric eruption.

Hemorrhagic bullous cases of extensive distribution are frequently fatal, 7 out of 11 quoted ending fatally. Petechial, non-bullous cases rarely terminate in death, unless there is marked disease of the heart or kidneys or a very extreme intolerance to the drug; 2 out of the 50 cases of this type ended fatally. F. C. Knowles (Jour. Amer. Med. Assoc., July 9, 1910).

A man of 65 with signs of amyotrophic lateral sclerosis was given potassium iodide and his temperature soon rose to fever heat. The iodide was discontinued, after which the temperature subsided to normal; but it rose again each time iodine in any form was given except by percutaneous cataphoresis of iodine salts. The thyroid was persistently normal. In a second case a woman of 33 presented the clinical picture of acute circumscribed thyroiditis on two occasions. It was learned that each had followed the local application of an iodine salve without medical advice; the thyroid was slightly enlarged. Konried (Med. Klinik, June 25, 1911).

In a friendly scuffle a young man was scratched by a finger-nail on the left side of the neck. The area was painted with tincture of iodine, no further dressing being employed. Next day the area over which the iodine had been applied was raised, reddened, and indurated, its general appearance being suggestive of ringworm. This was excluded, however, by the absence of itching and its development overnight. Erysipelas was thought of, but there were no constitutional symptoms, local warmth, or lymphadenitis. Tincture of iodine, 1:10, was then applied and the area left uncovered. Next day, the area was sloughing superficially, with a

copious serous discharge. The patient stated a blister had formed and broken during the night. A smear showed very few organisms, namely: staphylococci and bacilli, but no streptococci. The area was lightly curetted while being irrigated with an aqueous solution of iodine, 1:1000. Sterile gauze was then applied which the following day was soaked with serous discharge. The erythematous area was greatly extended, involving the adjacent portions of the scalp over which the iodine solution had trickled. Exfoliation and isolated pustules followed. Smears showed immense numbers of leucocytes, but no organisms. An area of the right forearm was painted for experimental purposes, with similar results. A. G. Wilde (Military Surgeon, Sept., 1913).

Case of gonorrheal epididymitis in which 15 grains (1 Gm.) of sodium iodide was injected intravenously. Next morning there was marked swelling of the left upper eyelid. The salivary glands were enlarged and there was difficulty in opening the mouth, because of pain. The hands and forearms showed an extensive erythematopapular dermatitis, with itching and burning, and later some serous exudation. There was violent headache with nausea, chills and vomiting. The symptoms were apparently ascribable to the intravenous administration rather than idiosyncrasy, since tincture of iodine had previously been applied to the skin without reaction and subsequent ingestion of 2 grains (0.13 Gm.) of sodium iodide had no effect. L. Isacson (Jour. Med. Soc. of N. J., Feb., 1924).

Thin has ascribed purpuric iodide eruptions to complete destruction of small areas of the vessels, and has demonstrated histologically a limited lesion of this kind.

Iodism has been ascribed to liberation of iodine from its compounds by some oxidizing agent in the body, nitrous acid, carbonic acid, the sebaceous secretion, etc., but there ap-

pears to be no satisfactory evidence supporting this view.

In occasional cases, especially of syphilis, potassium iodide may suddenly produce intense edema of the glottis, so severe as to necessitate immediate tracheotomy. In a series of 9 such cases collected from the literature by Groenouw, 4 patients had presented the edema on the first day, 1 under a dose of 15 grains, 2 under $7\frac{1}{2}$ grains, and the fourth under as little as 3 grains. All other symptoms of iodine were absent from these cases and after the disappearance of the edema persistence in the use of the drug produced no unfavorable effects. The likelihood of the occurrence of this edema is diminished by copious ingestion of water when the iodides are taken.

Salivation by mercurials may be either lessened, initiated, or increased by potassium iodide (E. B. Allan).

Atrophy of the mammary glands or testicles has been observed after prolonged use of iodine or its salts.

In some cases the nervous system exhibits the chief untoward action of iodine. Twitching of the muscles, neuralgic pains in the trunk and limbs, mental disorders, insomnia, hypochondriasis and hysteria have also been noted. At times the neuralgia is sufficiently severe to necessitate discontinuance of the remedy. In rare instances, paralysis of the sphincter muscle of the iris and of the ciliary muscle may be observed.

Another group of cases of intoxication comprises those in which there has already been present a latent or manifest tendency to thyroid overactivity. Pre-existing symptoms of exophthalmic goiter are likely to be aggravated by iodine preparations

(except for the temporary improvement which has been availed of for pre-operative preparation of such cases), and many authors have shown that prolonged use of iodides may in itself provoke exophthalmos. Römheld has reported a number of cases in which, because of incipient or feared arteriosclerosis, iodine had been administered and serious symptoms suggesting exophthalmic goiter had followed.

Case of secondary syphilis in which even small amounts of potassium iodide caused a considerable swelling of the thyroid gland with each successive dose. Remarkable about the case was the abeyance of all other symptoms of iodism. Csillage (*Wiener med. Woch.*, Nu. 33, 1905).

A woman of 52 years, four days after taking 20 c.c. ($\frac{2}{3}$ ounce) three times daily of a 5 per cent. potassium iodide solution, developed a well-marked uniform swelling of the thyroid gland. On stopping the medication the swelling subsided and on resuming it the enlargement promptly reappeared. Lublinski (*Deut. med. Woch.*, Feb. 22, 1906).

Case of a man of 47 years suffering from fatigue, anorexia and emaciation. A month later he was found very pale, with pulse rate 120 to 140, blood-pressure 140, temperature 37.8° C. (100° F.), and no other noteworthy findings. The symptoms grew worse, with dry throat, sleeplessness and disappearance of the hair on the chest. The patient stated that in previous years he had used iodine ointment for a small parenchymatous goiter, which had disappeared. He had not used the ointment for 2 years, but for several months he had been using irrigations of Pregl's iodine solution for pyorrhea alveolaris. Upon cessation of this, with injections of an arsenical preparation, his symptoms disappeared. Evidently even the external use of iodine in goiter involves some danger. Friedmann (*Münch. med. Woch.*, Sept. 22, 1922).

Case in which a small amount of iodine produced severe symptoms of hyperthyroidism and death in a woman, aged 27, who probably had had goiter, although during each of 2 pregnancies a visible goiter had disappeared under iodine treatment. The author disapproves of iodine therapy for hyperthyroid goiter in spite of its occasional successful use, since it jeopardizes the life of the patient. O. Roth (*Schweiz. med. Woch.*, Aug. 14, 1924).

Attention has been directed by Comby to the fact that iodism develops only exceptionally in children; the younger the patient, the less the likelihood of its occurring. This is due to the rapid elimination of iodine in childhood.

PROPHYLAXIS.—Administration of iodides in ample dilution and in small initial dosage is one of the chief safeguards against iodism. The use of milk as a vehicle is also, perhaps, a useful preventive measure. Rohmann and Malachowski found that simultaneous administration of potassium iodide and sodium bicarbonate failed to provoke iodism in cases where the ingestion of the former alone promptly induced it.

According to some the best agent for preventing iodism is arsenic in the form of Fowler's solution, 2 to 4 drops given during meals in water, with the iodides administered after meals in considerable water. Ammonium carbonate, bromides and belladonna have been extolled by other writers, but these agents are likely to provoke unpleasant symptoms when administered for a prolonged period.

The writer found that calcium given with iodides and bromides prevents iodism. This is due to the antagonistic action between calcium and the iodides and bromides. It can be studied on muscle fibers, the latter

drugs causing contractions in muscle fiber immersed in them, while the contractions cease when calcium is added to the fluid. E. Frey (Med. Klinik, March 1, 1914).

Brettonneau advises the employment of alkaline benzoates, preferably benzoate of ammonium, for the prevention of iodism. It may be given in cachets each containing 0.25 Gm. (4 grains), 4 to 8 to be taken daily.

Scrupulous cleanliness of the skin is said to be helpful in avoiding the iodic skin rash.

According to A. Hall, exposure of the skin to direct sunlight may contribute to perpetuating an iodine or bromide eruption after the drug has been stopped. In such cases the patient should remain in a dark room or, if need be, wear a red mask. Where the arms and legs are involved they should be dusted with a simple antiseptic powder or wrapped in a zinc oxide dressing.

The author has made it a practice for a long time past to have regular urinalyses made in patients undergoing iodide treatment; in most cases, even in young and otherwise healthy individuals, there were signs of renal irritation at times. Patients previously without a trace of nephritis showed albumin in varying amount and hyaline casts at times. He has seen a number of cases of permanent damage to the kidneys due to iodine medication. The great majority of cases of severe iodism have occurred in patients with renal insufficiency. Gottheil (Jour. Amer. Med. Assoc., Oct. 30, 1909).

Chronic alcoholics develop rhinitis and lacrimation even after 0.5 to 1 Gm. ($7\frac{1}{2}$ to 15 grains) of potassium iodide. Fifty alcoholics were given 1 to 4 tablespoonfuls of 40 per cent. iodide solution at intervals of 4 to 8 hours, i.e., 2 to 4 Gm. (30 to 60 grains) were given in 2 days as maximum. Distinctly positive results followed in 32 subjects, all of whom had marked rhinitis, lacrymation and nervousness; some had insomnia and 2 had iodide acne. Among the 18 negative subjects

were 10 syphilitics. Cold and damp weather yielded symptoms in alcoholics from small doses which had no effect in dry weather. The main predisposing factor seems to be the chronic irritation of the upper respiratory mucosa in alcoholics. An abnormal excitability of the salivary glands from alcohol abuse can be demonstrated with pilocarpine. M. R. Bonsmann (Münch. med. Woch., Dec. 30, 1921).

TREATMENT.—In the majority of instances the remedy need not be discontinued when iodism is produced. By reducing the dose the untoward effects may be sufficiently mitigated. It is to be borne in mind, nevertheless, that a number of cases have been reported in which progressively diminishing doses of iodide, administered at intervals, continued to induce iodism in spite of the reduced amount.

To relieve the coryza-like effects of potassium iodide, 5 drops of tincture of **belladonna** given with each dose of the iodide are efficient. **Sodium bicarbonate** in daily doses of from 90 to 180 grains (6 to 12 Gm.) has been asserted to relieve the general manifestations of the poisoning. **Sulphanilic acid** internally in doses of from 40 to 60 grains (2.6 to 4 Gm.) per diem has been claimed useful by fixing nitrous acid in the stomach.

Lombard prescribes as follows:—

R. Sulphanilic acid,
Sodium bicarbonate of each gr. viiss (0.5 Gm.).

M. et ft. in cachet. no. j.

Sig.: One cachet four times daily with meals.

Calcium lactate, 15 grains (1 Gm.) 3 times daily, and **Fowler's solution**, 3 minims (0.2 c.c.) in water after each meal, may be effective.

In addition, a diet poor in nitrates—milk, bread, and meats—may be in-

sisted upon. For the eruptions, anti-sepsis of the skin is important; baths and lotions of 1:25,000 **calcium permanganate solution** are useful. Hemorrhage should be treated with **ergotine** and salivation with **potassium chlorate** (Briquet).

ACUTE POISONING.—Ingestion of large doses of iodine is likely to produce at first a marked sensation of burning along the esophagus and in the epigastrium. Great thirst is complained of. A strong, metallic taste, as well as salivation, may also be early symptoms. Soon the irritant effect of iodine on the gastrointestinal mucous membranes asserts itself more strongly and there may follow nausea, vomiting, cramps and purging. There may occur tinnitus, shooting pains, diuresis and sexual excitation. After massive doses, these phenomena may be followed by marked prostration and circulatory depression, the pulse becoming thready and the skin very pale and cold, and later cyanotic. Anuria may exist; if, however, any urine can be obtained, it will be brown in color. The vomitus, containing iodine, is likewise tinged yellow. The later manifestations are increasing nervous excitement, convulsions, and finally a comatose state. Death, if it occurs, is due to respiratory failure; but it is seldom observed, the iodine readily combining with other materials to form non-irritating and easily eliminated compounds.

Bickel showed experimentally that iodine, or an albuminous compound containing it, tends to increase the flow of gastric juice and mucous secretion, *i.e.*, has the power to bring on "acid gastritis."

The quantity of iodine capable of causing toxic symptoms varies considerably in different individuals. While

doses as large as $2\frac{1}{2}$ drams (10 Gm.) have been taken without producing marked effects, 20 grains have been known to induce violent symptoms.

Case of acute and fatal iodine poisoning in a man, aged 70 years, suffering from arteriosclerosis, chronic interstitial nephritis, and hypertrophy of the left ventricle, and who ten years before had contracted severe syphilis. Administration of 15 grains (1 Gm.) of sodium iodide on 2 successive days was followed by iodism and iodine acne. On the same day there appeared subconjunctival petechiæ, swelling of the mucous membrane of the nose and throat, dyspnea, and enlargement of both testicles. Later the nares ulcerated. The urine contained albumin and hyaline and granular casts. No iodine was found in the urine. Three days after there occurred inflammatory infiltrations in the skin of the face and trunk, and a phagedenic ulcer formed on the lower lip. The skin of the trunk and extremities was covered with small abscesses and vesicles containing turbid, yellowish-green serum. This condition was followed by double hydrothorax, pulmonary edema, and death. The explanation given of the case was that, owing to the diseased state of the kidneys, the iodine was not eliminated, and the amount retained was sufficient to cause death in such a broken-down subject. Franz (Brit. Med. Jour.; Wiener klin. Woch., No. 23, 1899).

Report of the case of a man, aged 59, suffering from a swelling in the sternal region. As this was evidently gummatous, potassium iodide and liq. hydrarg. perchlor. (B. P.) were given; after three doses (amounting to 15 grains—1 Gm.—of the one and 2 drams—8 Gm.—of the other) the medicine had to be discontinued on account of violent vomiting. This having been subdued by lavage, the iodide was recommenced a week later. After taking 20 grains (1.3 Gm.) the patient was suddenly seized

with severe pains in the extremities. An extensive purpuric eruption rapidly developed, he became collapsed, and in thirty hours was dead. There was slight vomiting. *Post mortem*, recent ulcers—becoming gangrenous in places—were found in the stomach and small intestines, particularly the duodenum. The author considers that purpura is due to direct injury to the endothelial cells of the blood-vessels, and that in the case under notice it might have been due to the elaboration of a combined poison by the joint action of potassium iodide and a factor constructed directly or indirectly by tissue metabolism. J. B. Cleland (Brit. Med. Jour., July 11, 1903).

Toxic phenomena have been known to follow the application of iodine over mucous surfaces and its injection into morbid growths. Repin has reported 2 cases in which toxic absorption from tincture of iodine applied in the vagina took place; in 1 of these, symptoms of intoxication appeared in six minutes.

Iodides, apart from iodism, become acutely toxic only when ingested in large quantities. Even then their effect is for the most part limited to salt-action in the gastrointestinal tract, nausea and vomiting, occasionally with diarrhea, being the result.

TREATMENT OF ACUTE IODINE POISONING.—When this is due to free iodine the administration of **white of egg, milk, starch, or starchy foods**, such as **flour or arrow-root**, is indicated in order to fix the iodine and prevent its irritant action on the tissues; the first two antidotes named are to be given preference. Immediately after, the stomach should be evacuated by **lavage** or an **emetic**. **Opium** and **demulcents** may be given to allay pain and protect the mucous membranes. Where a tendency to collapse becomes manifest, stimulants

such as **aromatic spirit of ammonia, caffeine, strychnine, digitalis, and alcohol** should be administered, preferably hypodermically, and **external heat** supplied. To relieve iodine skin lesions **crushed ice** affords relief.

For iodism the writer gives **adrenalin**, at least 0.006 Gm. ($\frac{1}{10}$ grain) a day, in 2 doses, and if this prove insufficient, subcutaneous or intramuscular injections of 0.001 or 0.002 Gm. ($\frac{1}{10}$ or $\frac{1}{2}$ grain). It may be used also for the prevention of iodism. G. Milian (Paris méd., May 5, 1917).

THERAPEUTICS.—In **syphilis** iodine in the form of potassium iodide may be said to be an invaluable remedy in the tertiary stage and for visceral, osseous and nervous manifestations of the disease. An exception to the rule that it is required only for late syphilis is to be made, however, in congenital syphilis in the newborn, in which the exhibition of potassium iodide should be begun early (Comby). Not only should positively syphilitic children receive iodine, but all who present suspicious symptoms, such as coryza, exostoses, etc., or cachexia appearing without apparent cause, are prematurely born, or whose mothers have had frequent miscarriages. It may also be used in the presence of meningeal symptoms, convulsions, pseudoparalysis, **hydrocephalus**, etc. In children with gummatous tumors, bone disease, perforation of the soft palate, etc., its administration is, of course, clearly indicated.

In general the iodides must be exhibited in full doses if satisfactory results are to be obtained. The best plan is to give ascending doses, beginning, in adults, with 10 grains (0.6 Gm.) three times a day, and gradually augmenting the dose by 1

grain (0.06 Gm.) a day until the limit of tolerance is reached. Many patients attain 1 dram (4 Gm.) or more, especially if water is copiously taken at the same time. Huhner even had 2 patients taking between 500 and 600 grains daily without any untoward symptoms.

While the iodides have been less used and have lost some of their importance as antisypilitics since the introduction of arsphenamin and bismuth, there are many who protest against the statement sometimes heard that iodides are no longer necessary in the treatment of syphilis. According to Dix, *e.g.*, while not spirillicidal, they are, nevertheless, valuable allies to drugs possessing this property. Irvine approves of the use of potassium iodide in the rest periods between courses of the other remedies. Many also use it in conjunction with the other agents. Mulot, however, is opposed to its routine use, believing that it lowers the patient's tolerance of mercury. A particular field for the use of iodides is that of visceral syphilis, but they are not to be considered alone as sufficient for any case. According to Groedel and Hubert, they are indicated, in such cases, before or in combination with the treatment by metals, only in definitely demonstrated gummatous or recent inflammatory manifestations.

The iodides have no direct antisypilitic action, but are essential in all stages of the disease. Large gummas disappear rapidly under their influence, and a similar effect is produced upon the spirochetes in primary and secondary syphilis. The drug can be used with benefit at some period in every case of syphilis. The writer uses only the potassium or sodium salts in a dose of 15 grains (1 Gm.) 3 times daily, sometimes increased in tertiary

cases to 20 or 30 grains (1.3 to 2 Gm.). Intolerance of these doses is rare, and can usually be immediately overcome by administration of a single dose of 120 grains (8 Gm.) of sodium iodide intravenously. W. R. Snodgrass (Glasgow Med. Jour., June, 1924).

In 2 cases of late articular syphilis, refractory to other measures, the writer had excellent results from *intra-articular injections* of 0.2 to 1 c.c. (3 to 16 minims) of 10 per cent. sodium iodide solution, using a fine needle. In one case the apparently ankylosed wrists and severely involved knee were promptly mobilized by the injections. Pain from the injections was slight. The blood Wassermann is negative in most of such late syphilitic joint affections, but the puncture fluid may be positive. H. Schlesinger (Wien. klin. Woch., June 26, 1924).

In tuberculosis accompanying syphilis, iodeol and colloidal iodine preparations are useful. Potassium iodide must be used cautiously in such cases, initial doses of 0.2 to 0.3 Gm. (3 to 5 grains) being gradually increased daily by 0.05 to 0.1 Gm. ($\frac{1}{4}$ to 1 grain) until a dose of 2 Gm. (30 grains) daily may finally be tolerated. Mouradian (Ann. des mal. vén., Sept., 1924).

The *modus operandi* of iodine and iodides in resolving gummata and other forms of chronic inflammatory tissue is by no means definitely known. The proteolytic theory of their action is given most credence, and is supported by the febrile manifestations sometimes observed after the giving of iodides. According to this theory, union of potassium iodide with antibodies already present in the infected individual gives rise to a ferment which has the power of digesting certain proteins (granulomatous cells, etc.); in this process toxic substances are formed which create local inflammation in the lesion and at times a general febrile reaction (Capps).

Liénaux and Huynen have reported having found that iodides bring about marked hyperemia in the vicinity of tuberculous lesions in cows and guinea-pigs (likewise in patches of chronic eczema and scabies in dogs), and likened the action of iodides to that of a Bier hyperemia acting locally in pathological foci, the result being an afflux of blood, increased exudation and diapedesis, and more active phagocytosis. In tuberculous foci the relative paucity of vessels and great resistance of the tubercle bacilli to the action of leucocytes diminishes the probability of a favorable effect of the iodide on the lesions, but in other granulomata these factors are less prominent and the efficiency of the salt correspondingly greater.

Potassium iodide has also been credited by some with exerting an antiseptic effect in syphilis and other infections.

In **actinomycosis** the efficiency of iodides in promoting resolution of pathological tissue is practically as great as in tertiary syphilis. Doses of 15 to 30 grains (1 to 2 Gm.) a day are sufficient to produce marked curative effects.

In the writer's 4 cases of **actinomycosis**, 5 to 10 minims (0.3 to 0.6 c.c.) of tincture of iodine in a half cupful of milk 3 times daily proved sufficient to cure the patients. Chitty (Brit. Med. Jour., Feb. 27, 1926).

In **blastomycosis** (**oïdiomycosis**) favorable results have been reported from the intravenous use of potassium iodide. Senn reported a case in which internal use of this salt failed, but covering of the ulcerated surfaces with a compress of 1 per cent. solution of iodine and potassium iodide, aided by cataphoresis in daily

sittings of 10 to 15 minutes, brought permanent healing.

Intravenous use of 100 c.c. of 8 to 15 per cent. (usually 10 per cent.) sodium iodide solution acts rapidly in **oïdiomycosis** (**blastomycosis**). The solution is autoclaved, boiled and cooled before use, and given by gravity. This hypertonic solution is asserted to reduce the idiosyncrasy toward iodism. The writer also considers that iodides intravenously in concentrated form help the action of arsphenamin on diseased tissues and cells. F. J. Farnell (Arch. of Neur. and Psych., June, 1922).

In **arteriosclerosis** potassium iodide is believed, upon prolonged administration, to overcome, in a measure, vascular degeneration, promoting absorption of the cellular infiltration in the vessel walls and thereby enlarging their lumen or improving their elasticity. While this applies especially to cases of **syphilitic endarteritis**, good results are also considered obtainable with the drug in non-specific forms of arteriosclerosis. Vierordt, a champion of the iodides in this condition, begins with doses of only 2 or 3 grains (0.13 to 0.2 Gm.) two or three times a day, and then increases to 15 grains (1 Gm.) thrice daily. This is kept up for eighteen months to three years, with occasional intermissions, and the results thus obtained are claimed to have been very good in all forms of arteriosclerosis. Promotion of the elimination of irritants and waste-products by potassium iodide has also been held responsible for its favorable effects in arteriosclerosis. That any direct effect on the blood-pressure in these cases is exerted is to be doubted. Diminution of the viscosity of the blood may, however, be an operative factor.

Effect of iodine upon viscosity of blood studied in 12 patients with arteriosclerosis and hypertension. A very definite diminution in the viscosity followed in 8 cases. The arterial tension fell during the treatment, as much as 65 mm. of mercury in some instances. The same results were obtained in rabbits with the iodides of sodium or potassium. The blood viscosity increased or diminished parallel with increase or decrease in the number of red blood-corpuscles. There seems to exist a parallelism between arteriosclerosis, viscosity of the blood, and response of the case to treatment. Boveri (*Presse méd.*, Aug. 15, 1909).

Iodides have a marked hypotensor action in high blood-pressure without arteriosclerosis; in advanced arteriosclerosis with high blood-pressure they have no such action. To produce a beneficial effect in excess of tension, 10 grains (0.65 Gm.) of potassium iodide should be the initial dose. This should be rapidly increased if necessary. Matthew (*Edinburgh Med. Jour.*, March, 1911).

The iodides diminish blood viscosity and thereby facilitate circulation, according to Mueller. This action has been denied by some authors, and is doubtless inconstant, but in 1922 Deusch and Frowein observed it again in 72 per cent. of subjects who ingested 0.5 Gm. (7½ grains) daily of sodium iodide for 15 days.

It has been generally believed that iodides lower blood-pressure in a slow manner. All observers agree as to the absence of any immediate hypotensor effect. In normal man as well as animals even the tardy effects are inconstant. Dosage and individual susceptibility certainly play an important part.

Pouchet has observed that in some cases of disease therapeutic doses lower the blood-pressure, while in healthy subjects there was little effect from such doses, and the delayed hypotension took place only with larger amounts. There are no positive experimental observations as to

the effect of prolonged use of iodides on the blood-pressure. With the iodized fats a hypotensor action has been reported, but only in cases of hypertension due to certain drugs, such as ergotoxin. Tiffeneau (*Monde méd.*, Oct., 1923).

In cases of **aneurism** the favorable influence of potassium iodide is ascribed by Burnet to promotion of clotting in the sac, contraction of the sac then resulting from the formation of a firm clot. The iodides might also do good by eliminating poisons responsible for the arterial degeneration and removing from the vessel coats pathological material, thus restoring elasticity and permitting of contraction of the sac.

Angina pectoris is another of the circulatory conditions in which potassium iodide has proven of value. For it to be of real service, 30 to 60 grains (2 to 4 Gm.) a day should be given, and this should be kept up for months (Burnet). Sclerosis or spasm of the coronary vessels may perhaps be alleviated by the drug, and its beneficial action thus accounted for. Sodium iodide is preferred by Fränkel to the potassium salt.

In various affections of the respiratory tract iodides have proven of considerable service. In **bronchial asthma** they may be relied on to produce good results in most instances. Fairly large doses, for some time, are recommended. An efficacious combination is the following:—

R. *Potassium iodide* ʒij (8 Gm.).

Water, enough to dissolve the iodide.

Then add

Tincture of belladonna-

leaves ʒij (8 c.c.).

Syrup of orange-peel,

enough to make ʒiij (90 c.c.).

M. Sig.: One teaspoonful every three hours.

In **chronic bronchitis**, especially in the elderly, the iodides are not infrequently useful. According to Burnet, if ordered half an hour before meals, they should be taken in a small amount of water, not a glassful. The ingestion of a single large dose of 15 grains (1 Gm.) before bedtime is also recommended. Any gastric disturbance brought on may be relieved by combining ammonium carbonate with the iodide. E. B. Allan points out that even small doses may in some individuals aggravate bronchitis instead of relieve it, causing congestion of the mucous membrane and dyspnea. The drug is thus probably not to be considered applicable to all cases. Externally, iodine liniment may be painted over the chest with advantage in chronic bronchial catarrh.

Iodipin is preferred by Burnet to the inorganic iodides for employment in respiratory diseases, as it produces a more uniform effect. The 10 per cent. strength can be given in 1- or 2-dram (4 or 8 c.c.) doses, mixed with a little warm milk, three times a day; or, tablets of solid iodipin can be prescribed. It should be given on an empty stomach to obtain the most benefit. In cases of **pulmonary fibrosis** with distressing cough and difficult expectoration, most marked early in the morning, good results are obtained by giving a full dose of iodipin at bedtime.

In chronic diseases of the respiratory system only two or three remedies may be absolutely relied on, and one of these is potassium iodide. In **pulmonary fibrosis** as met with in stone-masons, the two drugs which proved of most value were iodide of potassium and ichthyol. With these two remedies alone the author was

often able to alleviate the symptoms very materially. When the dyspnea which in such cases generally results from emphysema becomes marked, iodides given regularly over a somewhat prolonged period almost always afford relief. Burnet (*Lancet*, Sept. 8, 1906).

In **pulmonary tuberculosis** iodine has been recommended, but it is doubtful whether it is productive of much benefit. Inhalations of its vapor, with or without admixture of turpentine, have been extolled as stimulant to the mucous membranes where there is profuse expectoration (likewise in **laryngeal tuberculosis**). The danger of hemoptysis is, however, probably increased by the systemic administration of iodine in any form in lung tuberculosis. In the early stages, local application of iodine over the threatened or diseased area is, on the other hand, of great service. The front and back of the chest may be painted on alternate days. The application of cotton wadding over the painted areas tends to increase the efficacy of the treatment. Intrathoracic injections of iodine have also been used in pulmonary tuberculosis.

[Although the cases were more or less advanced, and other methods had afforded but little encouragement, very distinct amelioration of their condition was obtained. The injections were well borne: no hemorrhage was caused, even where hemoptysis had previously occurred. Two of the patients were children, aged 4 and 10 years, respectively. The solution preferred by d'Amico (*Lancet*, March 29, 1913) consisted of iodoform, 1 Gm. (15 grains); camphor, 2 Gm. (30 grains); guaiacol, 5 Gm. (75 grains); essence of peppermint, 30 drops,—a quantity we deem excessive and needlessly irritating,—and olive oil, 20 Gm. (5 drams). The needle, preferably of platinum-iridium, should be of fine caliber and from 3 to 5

cm. long. In adults from 20 to 60 injections were administered, according to the extent of the disease, while in the 2 cases in children 10 sufficed. One c.c. (16 minims) was the amount usually injected, but as much as 4 to 6 c.c. (1 to 1½ drams) were required for cavities. Avoiding the cardiac area and large vessels while introducing the needle into the appropriate intercostal space, the solution is injected directly into the affected pulmonary area. The most favorable region is that comprised between the second and sixth ribs on either side. The apex is best reached through the dorsoscapular intercostal space.

Of the tuberculous nature of the cases treated there could be no doubt. The injections caused disappearance of the tubercle bacilli from the sputum, gradual cessation of the fever and cough, all other physical signs being also gradually eliminated. Open-air exercise and the patient's daily vocations being in no wise interfered with, the cases progressed steadily toward recovery while earning their livelihood—a matter of vast importance when we realize that the majority of cases occur among those most exposed to infection, the working classes of our great cities.—S.]

Internally, Zielinski has pointed out that potassium or sodium iodide can be employed with advantage in persistent forms of croupous pneumonia and the pneumonia following or complicating influenza. Beginning on or about the twelfth day of the disease, doses of 23 to 30 grains (1.5 to 2 Gm.) may be ordered for adults, and proportionately smaller ones for children.

The writer has proved to his own satisfaction that as a result of *intravenous injection* of iodine, (1) a general hyperleucocytosis is produced; (2) **chronic ulcers** heal rapidly; (3) incipient **tuberculosis of the lung** is arrested; (4) cases of the second stage of tubercle of the lung are in many cases benefited; (5) **chronic bronchitis** is very much improved, and (6) cases of **corneal ulcer** are quickly cured. As the leucocytosis is permanent for some

months and the amount of iodine used is very small, the former is apparently the greatest factor in the effects. He injects either 1 to 2 c.c. of tincture of iodine, diluted to 10 c.c.; or, the same quantity of a solution containing 36 grains (2.3 Gm.) of potassium iodide and 24 grains (1.5 Gm.) of iodine to the ounce. The results from either of these solutions are identical. It is best to fill the syringe first with the solution, and keep the needle separate. The needle is sterilized with alcohol. The original iodine solution is diluted with the distilled water to 10 c.c. in the barrel of the syringe. The needle having been inserted in the vein, the barrel is at once fitted on, the assistant releases the twisted bandage previously applied and gently raises the arm, and the solution is slowly injected. As large a vein as possible should be selected. Thrombosis is likely to occur in small veins. If pain occurs during the injection, the latter is stopped until the pain passes off, then resumed. False punctures with these solutions do not destroy tissue, as with arsphenamin, causing only a transient swelling and inflammation. In nearly 1000 injections, 2 thromboses occurred; these are avoidable by never injecting a small vein and never allowing the patient to lie on the injected arm. The injections are repeated at intervals of 1 to 2 or 3 weeks, according to the patient's condition and the leucocytosis produced. W. W. Jeudwine (Indian Med. Gaz., Dec., 1923).

In so-called "**scrofulosis**," iodine serves a useful purpose. Lugol obtained a large proportion of recoveries by means of the solution bearing his name, as far back as 1828. Bazin recommended it especially in early manifestations, before the cervical glands were greatly enlarged and ulceration near at hand. In the **peribronchial glandular enlargements** often encountered in scrofulous children, the exhibition of iodine is frequently attended with considerable

benefit. The syrup of the iodide of iron, given in 5-drop doses three times daily, is especially valuable in this connection. As a matter of fact, all scrofulous glandular swellings, joint enlargements and osseous disorders are beneficially influenced by iodine used simultaneously by mouth and externally. Spolverini has even recommended intravenous injections of iodine in cases of scrofulotuberculosis and **sypilis** in infants. He uses a solution containing 1 Gm. (15 grains) of iodine and 3 Gm. (45 grains) of potassium iodide in 100 Gm. ($3\frac{1}{3}$ ounces) of distilled water. The maximum dose is 5 c.c. ($1\frac{1}{4}$ fluidrams).

Gianasso treated 20 cases of **osseous tuberculosis** in children by Durant's method of injecting an iodide solution of iodine. About 30 injections of 1 c.c. (16 minims) were given. All the cases were considerably improved and suffered no inconvenience.

In **surgical tuberculous disease**, the author's *modus operandi* is as follows: Operate and scrape as usual. Then thoroughly swab the cavity with iodine liniment (B. P.). A piece of cotton-wool twisted around the end of a probe forms a good swab. The liniment is applied every day. The application does not cause pain, except momentarily. Granulations do not become excessive. At the first application a thin piece of gauze is packed in lightly, but never at subsequent dressings. From the first there is given internally a mixture containing syrup. ferri iod. (B. P.), 1 dram (4 c.c.), and potassium iodide, 5 grains (0.3 Gm.), thrice a day. Tatchell (Brit. Med. Jour., Feb. 13, 1909).

In **chronic pleurisy** and **empyema** good results have followed injection of undiluted tincture of iodine into the serous cavity after evacuation, or daily irrigation of the cavity with a solution consisting of 6 grains (0.4

Gm.) each of iodine and potassium iodide in 1 pint (500 c.c.) of water. The liniment of iodine is also applied to the chest as a counterirritant in chronic pleurisy, to promote absorption of the accumulated fluid.

In **rheumatism** potassium iodide is a valuable remedy in the subacute and chronic forms of the affection. To give it during the acute or inflammatory stage is worse than useless. It may be used, however, in rheumatic pains devoid of inflammatory manifestations, such as lumbago, sciatica, and neuralgia following exposure. Its efficiency is greatly increased by the addition of colchicum. The following formula for such a combination can be recommended:—

℞ *Potassium iodide* ʒij (8 Gm.).

Water, enough to dissolve the iodide.

Then add

Tincture of colchicum-

seed ʒiiss (10 c.c.).

Syrup of orange-peel,

enough to make ʒiij (90 c.c.).

M. Sig.: One teaspoonful every three hours.

The writer gives sodium iodide intravenously. Doses of 10 or 20 Gm. ($2\frac{1}{2}$ to 5 drams) are tolerated by patients unable to stand the least quantity in the stomach. A 10 per cent. solution is used. He begins with 5 c.c. (80 minims), gradually increasing to 20 c.c. (5 drams), repeated daily or at longer intervals. Sodium salicylate and iodide, thus used, gave excellent result in **acute articular** and **muscular rheumatism** and for the pain in **chronic rheumatism** and **gout**. A little saline solution is injected between the injections of the sodium salicylate and iodide. Da Matta (Brazil-Medico, Oct. 14, 1916).

Combined administration of the iodide with sodium salicylate has been advised by Burnet, on the ground that while the latter causes elimination of

uric acid, the iodide prevents uric acid from combining with alkali in the blood. Small doses of potassium iodide—5 to 10 grains (0.3 to 0.6 Gm.) thrice daily—are sufficient in chronic rheumatism.

W. Carter reported a case in which only 5-grain (0.3 Gm.) doses of potassium iodide, taken at intervals of thirty-six to forty hours, sufficed to relieve **gouty pains**.

Subcutaneous injections of a dose not exceeding 0.02 Gm. ($\frac{1}{2}$ grain) of pure, desiccated sodium iodide, while without any action under normal conditions, are very effective in relieving **pain** of various sorts, as well as vascular or bronchial spasmodic conditions. This applies to **intercostal neuralgia** and the **neuralgia** accompanying **grippe**, the initial pain in **pleurisy** and **pneumonia**, **lumbago**, **sciatica**, certain forms of **headache**, and the pain arising from **sinusitis** and **iritis**. The measure sometimes proved effective in **cardiac palpitation**, the **dyspnea** of **asthma** and **emphysema**, **acute pulmonary edema**, **post-traumatic vertigo**, and conditions resembling **angina pectoris**. The most marked evidence of the sedative effect of the iodide was seen in cases of **acute tenosynovitis**, **anal abscess**, **quinsy**, and **mammary abscess**, in which the pain was so obtunded as to permit of sleep on the following night. In a few cases a febricula was observed to follow the injection of iodide. J. L. Champion (*Presse méd.*, Dec. 18, 1912).

Administration of iodine in various **infectious states**, including **tuberculosis**, **rheumatic** and **pseudo-rheumatic disorders**, **influenza**, **typhoid**, etc., recommended. In conditions running a slow course, gradually ascending doses are to be used, while in acute, serious disorders large amounts are given from the start. In cases of intermediate severity he gives 10 drops of the French official iodine tincture every hour in a cup of milk; if the

measure seems ineffective and either fever or hypothermia persists, the dose is increased to 12, 15, or even 20 or 30 drops an hour. Iodine, he states, greatly shortens convalescence from any sort of infection. Boudreau (*Jour. de méd. de Bordeaux*, Mar. 10, 1921).

Iodine increases the resistance of the organism to disease. Infectious processes increase the need for it. It is important that its use in **acute infections** should be restricted to such formulas as allow absorption without irritation to the mucosa. The ideal method is to give iodine in solution in a large volume of water with the least quantity of salts of iodine that is permissible. Ammonium iodide is probably the most efficient aid to iodine solution. The following formula proves very successful in combating disease processes:

R Iodi gr. xxx (2 Gm.).
Ammonii iodidi . gr. xx (1.3 Gm.).
Alcoholis f3ss (15 c.c.).
Glycerini .q.s. ad f3j (30 c.c.).

M. Sig.: One to 4 drops in a glass of water.

Iodine is valuable in **chronic toxemia** accompanying **focal infections** or intestinal anomalies. Relatively small doses should be given continuously as long as the focus of infection exists. The blood-pressure and excretory functions should be closely watched. Iodine is frequently a short route to relief from the effects of the exceptional load of physical strain. In such cases the dosage should be reduced to 1 or 2 drops a day, or 5 or 10 drops every 3 to 5 days. A. J. Quimby (*Amer. Med.*, May, 1923).

An ordinary attack of **malaria** with a week or 10 days' treatment often relapses. An attack treated with iodine does not relapse. In cases that resist oral treatment with iodine up to the 4th or 5th day, the author gives 1 or 2 intravenous injections of $\frac{1}{4}$ grain (0.015 Gm.) of iodine, which suffices to bring the temperature to normal and keep it there. The results obtained with iodine in a few cases in which the spleen was enormously en-

larged but malarial parasites were not found led the writer to try iodine in **kala-azar**, in which it yielded the happiest results. The solution used consists of iodine and potassium iodide, of each 6 grains (0.4 Gm.), in distilled water, 1 ounce (30 c.c.). Forty minims (2.5 c.c.) of this solution contain $\frac{1}{2}$ grain (0.032 Gm.) of iodine. This amount is administered intravenously on alternate days up to 5 injections, after which 10 drops of tincture of iodine are given by mouth 3 times daily for a week. The spleen shows marked diminution of size before the 5th injection. To complete recovery, nourishing foods and tonics may be given. J. J. A. Brachio (Indian Med. Gaz., July, 1923).

Local application of iodine over painful areas in chronic rheumatism, the surfaces being then covered with cotton wadding, is of great assistance in affording relief and accelerating recovery.

In **acute articular rheumatism**, Stabler applies an iodine plaster to the affected joint. A piece of zinc oxide adhesive plaster about 6 by 8 inches has a thin layer of absorbent cotton or lint spread on the sticky side, leaving a margin uncovered about $1\frac{1}{2}$ inches wide all around. The cotton is moistened with tincture of iodine, tincture of belladonna, and spirit of camphor, equal parts. The plaster is warmed, applied, and covered with flannel. If the pain is not controlled in twenty-four hours, one edge of the plaster is raised and more of the solution poured in, covering the leak with a fresh piece of plaster. Mercury is pushed internally and also a little acetanilide and salol given. Morphine is very seldom needed where this treatment is begun early. Even in **sciatica** these measures gave better results than other forms of treatment.

Many cases of enormously enlarged joints, due to **bursitis**, **synovitis** or **arthritis** sometimes resembling those of a tuberculous nature have promptly responded, in the writer's experience, to a few external applications of iodine. In many instances **pleuritic effusions** have been entirely absorbed

with the following mixture, applied externally for 3 to 10 days:

R *Tincturæ iodi*,
Guaiacolis,
Olei gaultheriæ,
 āā 3ij (8 c.c.).
Petrolati liquidi,
 q.s. ad 3iv (120 c.c.).—M.
 H. B. Sheffield (Med. Jour. and Rec., Dec. 16, 1925).

In **simple hypertrophic goiter**, iodine or iodides, given very early in the course of thyroid enlargement and in small doses, are sometimes productive of good results, though often, again, their administration proves a failure. Injection of iodine tincture in doses of 5 to 15 or more minims (0.3 to 1 c.c.) into the substance of the goiter has been availed of with benefit in the simple hypertrophic variety of thyroid enlargement. Inunctions of iodine ointments over the goiter have also been employed. Careful selection and supervision of cases are necessary to avoid the risk of exciting hyperthyroid symptoms.

In view of the inadequate effect of the usual iodine ointment in goiter, the author used a stronger one consisting of iodine and potassium iodide, 5 per cent. of each in petrolatum. This contains 8.8 per cent. of pure iodine, of which $\frac{7}{8}$ is excreted in the urine after absorption, thus avoiding harmful results. The goiter is anointed with this for 10 minutes every night. By the mouth he gives iodine tropon (the latter a preparation of animal and vegetable proteins) in tablets each containing 0.05 Gm. ($\frac{3}{4}$ grain) of iodine. These tablets are taken 2 or 3 times after meals and well masticated, so that the iodine will be in contact with the saliva a long time. The tablets are given for a week at a time only, the iodine ointment being used in the succeeding week. He believes the iodine has a marked effect only when in the nascent state. O. Lan-

gemak (Deut. Zeit. f. Chir., Mar. 5, 1923).

The writer, a Swiss, found that where endemic goiter was notably prominent, iodine was far less abundant in the air, water and animal foods than in other localities known to be practically free from endemic goiter. There was also a contrasting iodine content of the excreta of persons in the localities compared. The more normal conditions were always accompanied by a relative richness in iodine. In actual quantity the differences were, of course, minute, consisting of such amounts as 0.038 mgm. ($\frac{1}{1700}$ grain) of iodine in the daily intake of this element. T. von Fellenberg (Biochem. Zeitschr., clii, 141, 1924).

Sea air was found to contain 13 times as much iodine as the air in Paris, the seaweeds, etc., yielding iodine to the air with their spores and débris. This iodine in the sea air is in an organic form, which is assumed to be easily assimilated—a factor accounting for the tonic effect of sea air. As for the sea water, Gautier found 2.32 mgm. of iodine per liter. At the surface this iodine is in organic form, but at a certain depth is inorganic. Loir and Legangneux (Bull. de l'Acad. de méd., Mar. 24, 1925).

Warning against the promiscuous use of iodized salt, which has been found responsible for numerous cases of hyperthyroidism. Continuous use of iodine over a long period should never be prescribed for adults, and when its periodic use is prescribed, frequent observations of the pulse and weight should be made. Under no circumstances should iodine be given to adults with fetal adenomas, either with or without symptoms of hyperthyroidism, except for a short period preceding operation. In the occasional case in which there is temporary improvement, the patient will be lulled to false security, and eventually a marked overactivity of the gland will result if the use of iodine is continued. In an adult with a simple large colloid goiter or a large

colloid adenomatous goiter without fetal adenoma, iodine sometimes has remarkably beneficial results and may be tried, but only with extreme caution, as it is this type of goiter that may become suddenly and overwhelmingly active, so that what appears one week to be a wonderful clinical result may be a fulminating case of hyperthyroidism the next week, with a basal metabolic rate of +75 or 100, marked asthenia and a loss of 5 to 10 pounds in one week. C. L. Hartsock (Jour. Amer. Med. Assoc., May 1, 1926).

In **exophthalmic goiter**, or Graves's disease, the use of iodine has proven advantageous for the purpose of temporarily reducing the metabolic rate previous to partial thyroidectomy. (See GRAVES'S DISEASE, Vol. V).

Favorable results with iodine treatment in **anemias** have been reported by Holler. The red cells under this treatment were found to become larger and contain more proteins and hemoglobin. In 2 cases of pernicious anemia this author observed absence of iodine in the thyroid gland.

Parenteral administration of iodine in the form of mirion was found to cause in normal subjects an increased diameter of the red blood cells, an increase in their number and in the hemoglobin values, and a rise of the color index. The temporary decrease in resistance of the red cells, followed by an increase, points to an effect on the bone-marrow, although the increased hemoglobin formation in the erythrocytes is ascribed by the writer to the iodine itself. A similar rise of color index and cell count was observed after parenteral administration of thyroidin combined with iodides by the mouth. In thyroid dysfunction the red cells become more richly charged with hemoglobin. In pulmonary tuberculosis the hemoglobin charging of the erythrocytes through iodine failed to occur, because of deviation of the iodine into the tuberculous tissues.

In anemias due to bone-marrow dis-

ease iodine injection was likewise followed by increased size of the red cells and a rise in hemoglobin values, but the increased consumption of blood cells with the existing insufficiency of the bone-marrow causes a fall in the erythrocyte count. Only in especially favorable cases did pure iodine medication with careful dosage increase the red cells. Arsenic treatment given after iodine in severe cases brought the red cells back to normal; the iodine mobilizes the organism for the subsequent arsenic treatment, which is thus rendered useful in anemias previously resistant to it. Thyroid preparations cause increased erythropoiesis in the presence of a normal or insufficient thyroid gland—another useful fact for the treatment of cases of idiopathic blood disease. G. Hollar (Zeit. f. klin. Med., Sept. 20, 1923).

Among skin disorders, **erysipelas** in its early stages may be advantageously treated and even aborted by the application of iodine. Mario treated 40 cases with success by dipping a sterile swab in fresh 10 to 12 per cent. tincture of iodine and lightly painting over the surrounding healthy skin, then painting with another similarly prepared swab over the diseased area, and covering the whole with sterile wool; this was repeated as often as five or six times a day.

Case of a child 2 weeks old who contracted **erysipelas** after circumcision. The inflammation had already involved the entire lower extremities and had spread above the umbilical region. Two circles of iodine, 1 inch wide and 2 inches apart, were painted around the baby's body, above the line of demarcation. The erysipelas was promptly arrested in its advance, although a few weeks later several abscesses on the body required incision and drainage. H. B. Sheffield (Med. Jour. and Rec., Dec. 16, 1925).

In **acne**, **psoriasis**, **pityriasis**, **tinea**, and **lupus**, iodides taken internally

are frequently beneficial. For **tinea tonsurans** a combination of iodine with oil of wood-tar has been advised for external application, while in certain cases of **seborrhea** the local use of the tincture of iodine has been found particularly valuable. In **scleroderma** the use of an ointment containing iodine sometimes yields favorable results.

Too frequent application of iodine in **tinea tonsurans** produces intense inflammatory reaction. The following combination, however, meets all indications:

℞ *Tincturæ iodi*,
Olei ricini ʒiiss (14 c.c.);
Phenolis,
Olei petrolei
crudi ʒiij (8 c.c.);
Olei rusci, q.s. ad ʒij (60 c.c.).—M.

After clipping the hair close to the scalp the mixture is applied with a small painter's brush over the entire scalp, more thickly on the affected spots, once a day for 5 successive days. On the 6th day, the mixture is wiped off with cotton dipped in linseed or olive oil; the hair is clipped again and the scalp thoroughly but gently washed with tincture of green soap. The whole process is repeated for 3 or 4 successive weeks, whereupon the fungus has usually disappeared and new hair is appearing on the bald spots. This procedure arrested a virulent and obstinate epidemic in an orphan asylum. The treatment is advantageously followed by a few applications of sulphur ointment or a 2 per cent. solution of resorcinol and salicylic acid in alcohol and castor oil. An oiled silk skull cap is worn at night. **Tinea circinata** yields promptly to a few applications of undiluted iodine tincture. In **tinea unguium** the iodine has to be applied daily for several weeks, with the fingers preferably enveloped in cotton and narrow bandages. In very stubborn cases the above mixture has always been successful. Sheffield (Med. Jour. and Rec., Dec. 16, 1925).

To prevent pitting in small-pox Rockhill found iodine very efficacious. Upon painting over the individual pustule a 10 per cent. iodine and 90 per cent. glycerin mixture, the lesions dry up and the customary destruction of tissue and disfigurement are avoided. Pustules upon the face should be opened with a sterile instrument and then touched with iodine tincture.

Vomiting is a symptom sometimes amenable to small doses of iodine. For vomiting in uremia, 1 to 3 drops of iodine tincture may with advantage be administered in ice-water or in cold milk.

Externally, tincture of iodine is extensively used as a counterirritant. As such it may be said to have become a household remedy, and to be more or less beneficial in almost all painful ailments—including, *e.g.*, **chilblains**,—except where abrasions are present. When burning and itching are experienced, iodine applications should be discontinued until these symptoms disappear. As a rule, the surface covered by tincture of iodine should not exceed that represented by the two hands, lest manifest poisoning through absorption occur. Linossier and Lannois have pointed out the fact that absorption of iodine through the skin becomes much more active when the part to which it is applied is hermetically covered. Such absorption is too irregular in rate, however, to render iodine painting useful for systemic iodine treatment.

As **surgical antiseptic**, *i.e.*, for the disinfection of the field of operation, iodine has proven extremely effectual, and may, in fact, be considered a method of choice because its use

occupies the least time and is the least burdensome to the patient. Its action consists probably both in destroying superficial germs and, in some measure, germs in the deeper layers of the skin, and in inducing a surface hyperemia favorable to local defensive processes, including phagocytosis. An essential precaution in the use of iodine is to avoid all preliminary washing of the skin that will prevent the latter from being absolutely dry when the iodine is applied, as any moisture at the surface will not only, by causing the intercellular spaces to swell, prevent a thorough impregnation with the germicidal agent, but will tend to bring on a subsequent iodine dermatitis. Patients may be bathed the day before the operation, where this is practicable, but in emergency cases ether or alcohol alone should be used for cleansing purposes before the iodine is applied.

Grossich and Walther demonstrated that iodine has the power of penetrating deeply into the layers of skin. The spaces between these layers are occupied by the various forms of bacteria, fat, sweat, etc. The inter- and intra-cellular capillary and lymph-spaces all communicate with these layers of epithelium, and it has been shown that iodine penetrates into all these various clefts and openings. The alcohol of the tincture dissolves the fat, while iodine forms a chemical combination with the fatty acids of the skin, which is quickly absorbed.

Weak dilutions of iodine, even to 5 per cent. of the official tincture, thoroughly sterilize the surface of the skin after from two to fifteen minutes. While the inhibitive action of absolute alcohol is quite potent, this property is greatly enhanced by the addition of iodine to an equivalent of 5 per cent. of the U. S. P. tincture. Tincture of iodine diluted with an equal amount of absolute alcohol is reliable as a local application in prep-

aration of the skin or mucosa in any part of the body. Dilutions of less strength are unreliable if hairs or large hair-follicles are in the field of operation. The 50 per cent. dilution, if not carelessly applied, is not likely to injure the skin. Bovée (*Amer. Jour. of Obstet.*, July, 1911).

Although at first it was thought necessary to employ the tincture of iodine in full strength, further experience seemed to show that a 25 per cent. dilution of this tincture, that is, one made by adding 1 part of it to 3 parts of alcohol, thus containing a little less than 2 per cent. of iodine (the tincture containing 7 per cent.), is equally efficient, while possessing the advantages of not endangering the skin of patients very sensitive to iodine and of less expense.

By some, however, a 50 per cent. dilution or the pure tincture is used, and Sabbatani has shown that all irritation of the skin can be avoided by removing the excess of iodine, after its purpose has been accomplished, by swabbing the skin five or ten minutes after its application with a tepid sterilized 5 per cent. solution of sodium thiosulphate (hyposulphite), followed by the application of a layer of cotton, to be lightly pressed down and removed in a few minutes. With this procedure, moreover, discoloration of the skin from the contact of the iodine is almost entirely avoided.

When an operator violates his aseptic technique, he may restore asepsis by immersion of the hands in tincture of iodine mixed with an equal part of alcohol, and subsequent dipping of them in a 10 per cent. sodium hyposulphite solution. Chabanier (*Presse méd.*, Aug. 10, 1912).

In the process of sterilization by iodine, the latter is simply applied to

the skin upon the operative field during the induction of anesthesia.

Dry shaving before the operation should alone be practised. According to Shanz, the line of cicatricial union is narrower after iodine than after other methods of sterilization.

One can begin an operation two minutes after a single painting with iodine. The second application of iodine tincture is not absolutely necessary, as the number of germs is but very little further diminished. Of greater importance is it that the first application be energetically made. Complete eradication of bacteria in the skin is not accomplished. The method is not suitable in some cases, as in Basedow's disease and in Thiersch skin grafting, when, if iodine is used, the grafts will not hold. Noguchi (*Archiv f. klin. Chir.*, Bd. xcvi, H. 2, 1912).

In cases in which the use of a hot, wet dressing after an operation is contemplated, the employment of the iodine is fraught with danger, as under these circumstances there is considerable probability of a severe dermatitis developing even if the iodine has apparently been thoroughly washed off with alcohol before the dressings are applied. (*Wjssconsin Med. Jour.*, April, 1912).

In a series of 225 operations performed using the Grossich-Brunn method of iodine disinfection of the skin under unfavorable conditions, the author had only 4 cases of suppuration, or 1.7 per cent., while in 90 operations in which the older methods were employed, suppuration occurred in 15 cases, or 16.7 per cent. Pavlovsky (*Roussky Vratch*, June 9, 1913).

Though tincture of iodine is effective as a means of sterilizing the skin, it has its disadvantages. Should the intestines come into contact with it, adhesions will undoubtedly take place in the area exposed, due to its action as an irritant to the peritoneum; when tincture of iodine is used as a means of preparing the field, the

utmost care should be taken to avoid such contact by protecting the field beyond the abdominal incision by means of moist pads securely fixed in place, and under no circumstances should iodine or the tincture of iodine be introduced into the peritoneal cavity. Frank (*Amer. Jour. of Obstet.*, Nov., 1913).

In major operations the writer favors the use of iodine as an internal disinfectant. It is microbicide and antitoxic, stimulates the production of leucocytes and the functions of the glands, especially ductless glands, and tones up the vital functions in general. L. Boudreau (*Jour. de méd. de Bordeaux*, Jan., 1916).

Before gynecological operations skin disinfection with tincture of iodine is the procedure adopted by many, and the agent is also applied with success to the vagina before operations on this part. The vaginal walls may be held apart by specula, swabbed thoroughly with ether, and then with tincture of iodine. Care must be taken subsequently not to allow any of the iodine to remain in the vagina. In certain cases, such as those of uterine prolapse, owing to the great difficulty in securing an aseptic operative field, the work of sterilization may be commenced on the preceding day, and iodine applied a second time just before the intervention.

Fifty labor cases were prepared with benzine and iodine and 50 alternate cases with the author's soap and water, bichloride and alcohol technique. Twenty-one of the former series gave negative bacterial cultures before and after delivery as compared with 22 of the latter series. Thus, both methods were equally ineffective in procuring an absolutely sterile field. F. C. Irving (*Amer. Jour. of Obst. and Gyn.*, Feb., 1923).

Tincture of iodine rarely causes irritation of the surgeon's hands. It

can be removed from the latter by means of boiled or raw starch, ammonia water or the aromatic spirit of ammonia, sodium hyposulphite, hydrogen peroxide, Fowler's solution, or ether. Where long periods of operating are expected it is advisable to dip the hands in iodine, at once decolorize with ammonia, then slip on rubber finger cots, and redip in the iodine (Woodbury). Continued contact of iodine with instruments tarnishes and affects their cutting edges; the customary preparation by boiling is, therefore, preferable.

Iodine is decolorized in several ways: by the use of any of the alkalis, by phenol, by sodium thiosulphate, and by sodium sulphite, but in every one of these methods the iodine enters into combination, and thereby loses all or the greater part of the antiseptic power for which it is chiefly employed. The "colorless iodines" are useless for sterilizing the skin. Willmott Evans (*Lancet*, Jan. 7, 1911).

A chemical change rapidly takes place between sodium thiosulphate and iodine, the two chemicals blending to form sodium iodide and tetrathionate, which are both very soluble and readily wash off the skin and tissues. Snoy (*Deut. med. Woch.*, Jan. 26, 1911).

Catgut can be made aseptic through immersion in 5 per cent. alcoholic tincture of iodine or in a 1 per cent. aqueous solution of potassium iodide and tincture of iodine. The strength of the catgut does not suffer if the material is left for five days in the solution. It is of importance to use only catgut freshly immersed in tincture of iodine. Hoffmann and Budde (*Deut. med. Woch.*, March 28, 1912).

A solution consisting of iodine and alcohol alone rapidly deteriorates, with the development of the irritating hydriodic acid. If such a solution is

to be used in skin disinfection, therefore, instead of the official tincture containing potassium iodide, it must have been one prepared immediately beforehand. It may prove convenient to carry in a tightly stoppered vial 40 grains (2.5 Gm.) of iodine, to which, when required for use, 1 ounce (30 c.c.) of alcohol can be added, making approximately a 10 per cent. tincture.

The era of iodine as an antiseptic and disinfectant for **wounds** began with the observations of Grossich in 1908, though Carl Beck, in 1901, had already pointed out the value of the method and shown that no bacterial cultures could be obtained from areas thus treated. Accidental wounds rich in bacteria heal by first intention when their immediate vicinity is painted with the tincture.

In traumatic surgery tincture of iodine appears to the author to be the best of all antiseptics. In treating with it nearly 1000 patients with incised, lacerated, and contused **wounds, dog-bites, compound fractures, traumatic amputations**, etc., he has obtained excellent results. The more simple the technique, the better. T. G. Orr (Jour. Mo. State Med. Assoc., May, 1913).

Nascent iodine vapor for **sluggish wounds**, combining a thermocautery bulb apparatus with Jarret's urethral cannula and a small quantity of iodoform and a few particles of pure iodine, is used by the writer. The wound is first carefully treated with moist, aseptic dressings. A dry superficial layer forms under which healing rapidly progresses. Quinsac (Presse méd., May 13, 1918).

The technique for the use of iodine in lacerated or other wounds such as often arise in those engaged in industrial or agricultural occupations is described by Réclus as follows: With a gauze sponge held in forceps

and dipped in tincture of iodine, every recess of the wound should be coated with the tincture. Every crevice must be reached, even at the expense of enlarging the wound, if necessary. Next the surrounding skin is treated in the same way. Any excess of iodine may then be washed away with alcohol. The latter is then allowed to evaporate and as soon as the surface is dry, the wound covered with an aseptic pad and a layer of absorbent cotton, held in place by a light bandage. In twenty-four hours the dressing should be removed, iodine again applied to all recesses of the wound, and after drying, gauze and cotton again applied. This may be repeated daily until all oozing ceases, when the dressing need only be changed every three to five days. Where secretions collect under loosened skin or crusts, the latter should be removed and iodine applied. With this treatment preliminary preparation of the wound by washing and scrubbing is both unnecessary and prejudicial. It is merely necessary to dry the wound carefully before applying the iodine and, perhaps, to trim away skin or other tissues the vitality of which is plainly destroyed. The efficiency of this procedure, notwithstanding its simplicity, has proven far greater than that of the older methods of time-consuming cleansing and antiseptics, healing taking place with great readiness and with minimum loss of tissue. In all **crushes** of extremities and **compound fractures** Réclus highly recommends the employment of iodine. Stone considers a 25 per cent. dilution of the iodine tincture sufficiently strong for ordinary purposes in emergency cases.

The filthiest **wounds** may be cleaned up with gasoline, painted over with tincture of iodine, and wrapped up in dry gauze, and the surgeon can wait the outcome with an easy mind. Jack (Washington Med. Annals, Sept., 1911).

Puncture wounds caused by nails, etc., should be treated by enlarging the opening through the skin, cleaning out the wound with a small ear curette and introducing a narrow strip of gauze twisted and dipped in iodine. C. F. Nieder (N. Y. State Jour. of Med., April, 1911).

Alcohol to which crystals of iodine in excess have been added, "10 per cent. tincture of iodine," is an ideal and powerful counterirritant. Iodine hydrate (4 per cent.) is unrivaled for arresting **pimples, furuncles, and carbuncles**, and is a good skin antiseptic preliminary to hypodermic or intravenous medication. After application it fades quickly. Used in **wounds** it is relatively painless. Vinegar of iodotannic acid (acetum acidi iodotannici), made by rubbing up 1 ounce (30 c.c.) of U. S. P. tincture of iodine with 1 dram (4 Gm.) of tannic acid and 3 ounces (90 c.c.) of dilute acetic acid, acts powerfully in wounds or infected areas. It tends to harden and preserve catgut. It lends itself readily to use in the throat, vagina or urethra, though it is not a counterirritant. In **compound fractures and osteomyelitis**, dilute tannin solution may be applied through a fenestra in the splint, and paraffin purple run through the overlying gauze pads, iodotannic acid being formed. Paraffin purple is made by rubbing up with a little ether, iodine and potassium iodide, of each 40 grains (2.6 Gm.), calomel, 12 grains (0.8 Gm.), and adding slowly liquid paraffin 3 ounces (90 Gm.). This procedure is effectual in **burns, cellulitis, dermatitis**, and similar conditions. D. H. Stewart (Med. Rec., Sept, 28, 1918).

Iodine is used in **local suppuration**, including foul **ulcers, inguinal adenitis, tuberculous sinuses, chancroids**

(especially when **serpiginous**), etc., acting as germicide and deodorant. In most cases of **scalp wound**, Pugh has succeeded in obtaining primary union by first cleansing with normal saline solution, then thoroughly drying, swabbing the wound with the tincture, and closing it completely. Similar success was often noted in **inguinal adenitis** upon opening up the suppurating area thoroughly, swabbing it clean with dry sponges, applying iodine carefully to every part of the wound, and where the focus was not too extensive, closing it entirely. Réclus notes the iodine tincture as having a very favorable effect in preventing the extension of a **cellulitis**.

Subcutaneous infections, such as **boils, carbuncles, phlegmons, felons**, etc., are treated with the happiest results by combining ichthyol and tincture of iodine, of each 1 part, with 6 parts of boroglyceride. The author applies them on lint or absorbent cotton, and covers with parchment paper and a bandage. Also in **erysipelas** and in **mammary inflammations**. In **local infection of the uterus occurring after abortion or parturition** this method has given excellent results. Being harmless and painless the solution may be injected into the uterine cavity. The depleting action of the glycerin is here a valuable adjunct. Where the cervix and vagina only need treatment, the patient may be trusted to make the applications herself, as but a teaspoonful of the iodine, ichthyol, and boroglyceride, injected into the vagina and left there, 2 or 3 times a day suffices. Stabler (Med. News, June 25, 1904).

In **cold abscesses** in individuals with lowered resistance, the author found a sterilized glycerin or olive-oil emulsion of iodoform of great value. In **suppurative arthritis**, abscess cavities, and **empyema**, he used iodine in 1:1000 strength. For hand

disinfection he advises: Iodine, 2.5 Gm. (38 grains); potassium or sodium iodide, 5.5 Gm. (85 grains); water 250 c.c. ($\frac{1}{2}$ pint). This gives a 1:100 solution, which can be readily diluted as desired. Cannaday (Jour. Amer. Med. Assoc., April 14, 1906).

The author fills **abscess** cavities or **suppurating ulcers** with a 5 per cent. solution of iodine in ether. One application is ordinarily sufficient. The same treatment is adapted to **chronic fistulas**. If preferred, 10 per cent. iodine in petrolatum may be substituted, or gauze may be soaked in a 10 per cent. solution in ether and the cavity filled with it. Isambert (Gaz. des hôpitaux, 110, 1906).

In case of acute spreading **gangrene** starting from a puncture of a hematocoele, and which had invaded the belly wall, the thorax, and formed tympanitic pockets in the armpits, the author opened the major focus of infection with a thermocautery, evacuating gas which burst into flame. Iodine was applied thoroughly to the cavity and the patient recovered. Reclus (Presse méd., No. 13, 1911).

In the **skin infections** often seen in threshers, corn huskers, harvest hands and others, in which one center of infection, boil or abscess, is followed by a crop of others within a limited zone, no treatment is superior to lancing the abscess, opening the little yellow pimples, absorbing the contents with gauze, and applying iodine to the whole area. F. A. Long (Western Med. Rev., Oct., 1912).

Paronychia can frequently be arrested in its inception by the use of iodine. A few drops of the tincture are instilled in the nail-bed and well surrounded by a pledget of absorbent cotton and several strips of adhesive plaster. Usually only one dressing is required. This mode of treatment is particularly serviceable in diabetics, in whom surgical procedures are generally contraindicated. H. B. Sheffield (Med. Jour. and Rec., Dec. 16, 1925)

In various forms of mucous-membrane infection, iodine has proven im-

mensely helpful. Intravenous injections of sodium iodide have been recommended in various ophthalmologic conditions.

Sodium iodide intravenously—5 to 10 c.c. (80 to 160 minims) of a 10 per cent. solution every 2 or 3 days, or in acute cases daily—advocated in **syphilitic** and **tuberculous eye affections**, **hemorrhages** and **exudations of the vitreous body**, and in **detachment of the retina**. In children of 6 to 10 years the dose is halved. Metzger (Klin. Woch., June 11, 1925).

Iodine is frequently employed in **trachoma**, and, according to Woodbury, can be used in a dilute preparation in ordinary forms of **conjunctivitis**.

Iodine used in an ointment, with an anesthetic, as a **disinfectant of the cornea**, notably after the extraction of foreign bodies. The formula is: *Stovaine*, 0.15 Gm. ($2\frac{1}{4}$ grains), finely pulverized and dissolved in 5 drops of oil. Add, after mixing, preferably on a water-bath:—

Hydrated wool-

fat 5 Gm. (75 gr.).

Petrolatum 10 Gm. ($2\frac{1}{2}$ dr.).

Add gradually the following solution:—

Iodine 0.15 Gm. ($2\frac{1}{4}$ gr.).

Sodium iodide .. 0.30 Gm. ($4\frac{1}{2}$ gr.).

Water $1\frac{1}{2}$ Gm. (24 min.).

Dewaele (Trans. Belgium Ophthalm. Soc.; Ophthalmology, Jan., 1913).

Tincture of iodine is invaluable as an antiseptic in ophthalmology. There is no risk, as the tissues of the eye bear it perfectly. One or two drops of cocaine should be instilled beforehand to avoid pain, and the iodine applied directly to the seat of injury by means of a cotton pledget. It is particularly valuable in **affections of the lids**, in **corneal ulcers**, and for pre-operative and postoperative work on the eyeball. Many cases of injuries could in this way be successfully treated by the general practitioner. The author has for the same purposes

used it in 37 **cataract** operations, among others. Jacqueau (Lyon méd., April 27, 1913).

The writer emphasizes the absence of caustic action when tincture of iodine is applied to the eye. He has used it in 107 **cataract** operations without iridectomy and in 74 cases with iridectomy, and all were cured in 3 days. In 4 cases of hernia of the vitreous body all were cured in 4 days. He regards it as harmless for the eyeball; no signs of irritation are apparent when the eye is dressed the next day. Even the vitreous body does not seem to be injured by it, he says, while it wards off post-operative pain and promotes rapid healing. R. Guiral (Rev. de med. y cir., Havana, Apr. 25, 1918).

In nasopharyngeal affections, and likewise lachrymal disorders, weak solutions of iodine in glycerin are of great value when gently applied night and morning with a camel's hair pencil, or pledget of cotton. Inhalations of iodine (20 minims to 1 dram of the tincture in a quart of boiling water, inhaled for five minutes at a sitting) have been used in **chronic rhinitis**, **coryza**, and **hay fever**. Hunter Mackenzie advised applications of the pure tincture, after cocaine, in atrophic disorders of the nasopharynx, and specifically in **ozena**, nasal douching with saline solution containing a few drops of the tincture has been advised. Hugh Taylor saw good results from free application of the same preparation to the throat, as well as its inhalation, in **diphtheria**, though these measures are in most instances rendered unnecessary by the use of antitoxin. In intranasal **lupus** the employment of Pfannenstiel's method, consisting in the internal administration of moderate doses of potassium iodide and liberation from it of iodine *loco dolenti*

by the insertion of cotton soaked in hydrogen dioxide solution, is asserted to yield gratifying results. In **tonsillitis** applications of the tincture are useful.

A solution of 1 teaspoonful of iodine tincture to the quart of physiological salt solution is most efficacious as an irrigation in all inflammatory and **catarrhal conditions of mucous membrane**. It can be used in the eye for the ordinary forms of **conjunctivitis** with prompt improvement. The author has also found it very efficacious in **acute urethral gonorrhea** in twice or three times this strength. When a case of **mumps** developed in a company of infantry this solution was supplied to the company to be used copiously as a gargle for several days. No other case of mumps developed. It is a routine treatment for acute throat affections.

In **tonsillitis** the tonsils are mopped once daily with the tincture; this, with Bier's treatment with a rubber bandage around the throat, has cut down the illness to an average of five days.

The saline solution will promptly abort colds when used as a spray. It is excellent in **cystitis**, acute and chronic, and catheters kept in the tincture and then transferred to this solution just before use, are sterile, non-irritant and perfectly pliable. Cases of **chancroids** with **suppurative inguinal adenitis** are hurried to convalescence by a vigorous pursuit with the tincture. **Buboes** already broken down promptly become healthy, granulating wounds. F. T. Woodbury (New York Medical Journal, Dec. 3, 1910).

In certain superficial lesions, the author gives potassium iodide by the mouth and applies the electric current to the spot; nascent iodine is generated in the lesion, exerting its therapeutic power to the full. The patient, fasting, takes 3 Gm. (45 grains) of potassium iodide. Between one and two hours afterward the electricity is applied, the positive pole

being introduced into the skin while the negative pole, wrapped in a wet pad, is held in the hand. As the iodine is generated only close to the needle, the therapeutic action is enhanced by using five needles, each 0.5 mm. in diameter, soldered to a metal plate at intervals of 0.5 mm. The process was repeated two or three times on each patch of **lupus**. Reyn (Berl. klin. Woch., Oct. 16, 1911).

Cases of **severe sore throat in children** cleared up and healed in two or three days after local application of iodine that might have required a week for cure by other methods. Although pronounced burning or pain in the throat is produced by the iodine tincture, it does not last long and the good results justify the use of the remedy. Where a milder application than the tincture is desired for the throat, especially deep down in it, and in the nose, equal parts of glycerin and iodine tincture are satisfactory. This combination was used in babies only 1 year old with good results. H. M. Sill (N. Y. Med. Jour., Dec. 9, 1911).

Nascent iodine, liberated by the interaction of sodium iodide and hydrogen dioxide, used in aural, nasal, and laryngeal practice. After a cleansing irrigation of the parts with boiled water, 5 drops of an aseptic 3 per cent. aqueous solution of sodium iodide are instilled, followed immediately by a like amount of hydrogen dioxide solution, which is then allowed to act for ten minutes. These instillations are to be repeated daily or on alternate days. They cause a certain degree of burning, which is, however, always bearable.

In obstinate **purulent rhinitis**, as well as in **ozena**, after the parts have been cleansed with a tepid isotonic solution, a spray of a 30 per cent. solution of sodium iodide should be used, at once followed by one of hydrogen dioxide, from a different spray apparatus. About six bulbfuls of each spray should be used.

In pharyngeal affections, such as **lacunar tonsillitis** and **chronic pharyn-**

gitis, the solutions may be employed either as sprays, direct applications, or gargles. P. Laurens (Quinzaine therap., July 25, 1912).

A 1 per cent. solution of tincture of iodine in glycerin, preferably combined with 0.25 per cent. of phenol, often acts very efficiently in **chronic rhinitis** and **rhinopharyngitis**, and in **suppurating adenoids**. As in these cases the submaxillary glands are generally implicated, it is well to apply also a 5 per cent. solution of tincture of iodine in liquid vaselin to these glands. Tincture of iodine acts almost as a specific in **postoperative infection** after adenotonsillectomy, with persistent hyperpyrexia, undue sloughing, and symptoms of general sepsis. Often after one swabbing of the throat all the symptoms disappear. The application may be repeated once or twice a day for several days, if this proves to be necessary.

The spasmodic coughing and great difficulty in swallowing which occasionally result from **injury** or **infection** of the **uvula** during tonsillectomy are also quickly remedied by a few applications of tincture of iodine. In **tonsillitis** and cognate affections he prefers a mixture in equal parts of the tinctures of iodine and myrrh, 10 drops in a wineglassful of water to be used as a spray or gargle every hour or two. The same formula acts very beneficially in **stomatitis**, **pyorrhea**, and **gingivitis**, while in **alveolar abscess** the undiluted tincture of iodine applied *p. r. n.* is to be preferred. H. B. Sheffield (Med. Jour. and Rec., Dec. 16, 1925).

In the realm of otology favorable effects have been reported by Koenig from *iodine fumigation* in **chronic otitis media**. The procedure consists merely in vaporizing iodine by heat and introducing its vapors into the ear by means of a current of warm air.

Good results reported from blowing iodine vapor into the tympanic cavity in a case of **chronic otitis**

media in which the mastoid had been opened, but discharge of thick pus continued through the meatus. The apparatus used consisted of an ordinary flat ink-bottle, provided with a perforated cork through which were passed two short glass tubes, one connected with an atomizer bulb and the other leading through a rubber tube to a small, curved cannula. Before use, a small quantity of iodoform was placed in the bottle, and the tip of a thermocautery (or wire heated in a flame) brought near the iodoform to set free iodine fumes from it. E. Chapellier (*Arch. gén. de méd.*, Sept., 1912).

The action of iodine in **respiratory catarrhal conditions** is most intense when the tincture is painted on the chest near the mouth or nose, and the author, therefore, concluded that the best effects could be obtained by having the patients inhale directly the fumes of the tincture of iodine. His clinical observations have proven the value of the method. He calls especial attention to the fact that inhalation of the dry fumes of tincture of iodine is preferable to moist inhalations. The dry fumes penetrate deeper into the pulmonary air cells, leaving behind the alcoholic vapors, which are immediately taken up by the humidity of the air and eventually fixed to the mucous membranes.

In applying the measure, recently prepared tincture of iodine should be placed in a wide-mouthed bottle so that the patient's mouth and nose will not touch the glass. The inspirations, numbering from 4 to more than 8 at each sitting, must be more or less deep, according to the gravity of the case, and the inhalation repeated 5 or 7 times a day. An ordinary cold will thus be broken up in one day, but if the case should be in the nature of a **bronchial catarrh** it will take four days to cure it. If the mucous membranes are covered with a thick, mucous stratum, it is well to intensify the iodine treatment and assist expectoration by giving the usual remedies.

In children the treatment may be simplified by dropping the tincture of iodine on pieces of cotton laid on the pillow while the patient is sleeping. Staining of the pillow is avoided by placing a piece of oilcloth under the cotton. G. Torri (*Policlinico*, No. 31, 1913).

A study of the prophylactic and therapeutic use of iodine in acute infectious diseases of the upper air tract showed that iodine alone did not suffice to kill the bacteria, but that it seemed to prevent their further development. Either the nutrient medium was unfavorably affected for the growth of the bacteria or the iodine exerts a direct damaging effect on the bacteria themselves. The writer used the halogen in a 10 per cent. solution of potassium iodide [iodine, 0.3 Gm. (5 grains); potassium iodide, 3 Gm. (45 grains); distilled water, 30 Gm. (1 ounce).] For children up to 10 years of age the dose is 5 drops and for older children and adults, 8 drops. Finck (*Munch. med. Woch.*, Apr. 9, 1920).

In stomatology, iodine is used for the purpose, among others, of stimulating the gums where they tend to become retracted in the elderly. Stillé recommended, to this end, that a dilute aqueous solution of iodine (gr. j- $\overline{5}$ j) be painted on and the mouth then at once rinsed with water. In dentistry, the tincture is found useful to remove tartar from the teeth, and when evaporated to one-fourth its volume ("dental tincture of iodine") is employed as a counterirritant in cases of inflammation of the dental pulp or the pericementum, as well as to deodorize putrescent cavities in the teeth. In **pyorrhea alveolaris** Lugol's solution is frequently used.

A double decomposition of mercury and iodine compounds with the formation of nascent mercuric iodide can be utilized therapeutically in

cases of **tuberculosis of mucous membranes—buccal, laryngeal, and cystic**. Especially in **tuberculosis of the bladder**, excellent results are obtained. The patient is given a teaspoonful of a 5 per cent. solution of potassium iodide $\frac{1}{4}$ hour before local treatment, which consists of insufflation of calomel or its injection in oily emulsion. Hollander (Berlin Soc. of Med., May 16, 1906).

In **chronic cystitis** Pregl's iodine solution was found to act well as a local antiseptic. The bladder is first washed clean with 2 per cent. boric acid solution, and this is followed by injection of a mixture of equal parts of Pregl's solution and 2 per cent. boric acid solution. Upon intravenous injection of Pregl's solution, iodine was demonstrable in the urine in 5 minutes. In persons with healthy kidneys the total time of excretion averaged 50 to 60 hours. W. H. Jansen and H. Näher (Münch. med. Woch., July 7, 1922).

In soiled fresh **wounds**, prophylactic use of Pregl's solution proved very effective. In **furuncle** and **carbuncle** the lesion may be advantageously covered after incision with compresses dipped in this solution, to be changed several times daily. **Abscesses** may be punctured and filled with it, or may be freely incised and the incision loosely packed with tampons wet with this solution. In the former case either rapid healing follows or there is an increased inflammatory infiltration which prevents further use of the solution; in the latter case there occurs decreased secretion and good formation of granulations. In other suppurative conditions, irrigation with Pregl's iodine solution or the application of loose tampons dipped in it cause lessened secretion from the wound and quicker subsidence. O. Specht (Beitr. z. klin. Chir., cxxx, 621, 1924).

J. Wesley Bovée confines the treatment of **acute and chronic gonococcal infection** of the female lower generative tract to the application of iodine.

If the condition, he states, can be treated before the infection has entered the uterine cavity or Bartholin's glands, it can often be eradicated by one thorough painting of the exposed areas below the uterine cavity. Where the first application fails, a second, made three days later, will commonly succeed. Some patients may be somewhat irritated by the iodine, but in the majority it may be used fearlessly about the vagina and perineum. Anything less than a 50 per cent. dilution of the tincture will only inhibit for a time, not kill, cultures. In the radical operation for **cancer of the cervix**, infection of the peritoneum as a result of rupture of the specimen during its removal is best obviated by the application of iodine to both the vagina and endometrium (preceded by galvanocauterization, with or without curetment, if excrescences or craters have been present).

One of the best treatments for **gonorrheal urethritis**, acute or chronic, anterior or posterior, is a solution of iodine and potassium iodide, 1 part of each to 100 parts of water, for injection or irrigation of the urethra. In the acute cases there should usually be given internally potassium iodide and potassium bromide, 5 grains (0.3 Gm.) of each, well diluted with water, every four hours.

There is no simpler or better treatment for **furunculosis** and **carbunculosis** than to paint, in the early stage, externally the neighboring vascular area with iodine tincture, to inject a few drops hypodermically into the tumor masses, or to drive a solution into the swelling by cataphoresis, and then institute free purgation.

In treating **ringworm**, one may dissolve metallic iodine with alcohol and ether, add collodion and apply. H. H. Stromberger (Amer. Jour. of Dermat., May, 1911).

Iodine *in statu nascendi* used as a disinfecting agent. The author first applies a few drops of a 5 per cent. solution of potassium iodide, then irrigates with a 0.1 to 1 per cent. solution of perhydrol. The disinfecting powers of the latter can be increased by adding some citric or lactic acid. Excellent results were seen in persistent subacute or chronic gonorrheal urethritis. The injections must be made before urinating and only small amounts of the iodide are to be used. Instead of the perhydrol, one may employ a solution of sodium perborate. The most brilliant results were seen in suppurating lacunæ or erosions in **subacute or chronic gonorrhea** of the pars anterior, the applications being made through the endoscope. Ten to fifteen minutes after the application the patient is instructed to urinate. Strong solutions may be employed in this condition without doing any harm. The treatment may also be used in **chronic endometritis** and **erosions of the cervix of gonorrheal origin**. R. Kaufman (Berl. klin. Woch., Dec. 11, 1911).

In conservative **surgery of the uterine appendages** the author uses force in applying iodine to every irregularity of the cavity of the uterus, and if possible to the tubal mucosa by way of the uterine cornua. The cervix is seized with volsellum and gently dilated. A 2-ounce glass syringe with conical nozzle about two inches in length is used to apply the iodine. About an ounce of diluted tincture of iodine (25 per cent.) is drawn into the syringe and the uterine cavity is filled and distended with all the force the syringe will permit. This pressure is continued for about two minutes.

The patient is now placed in the high pelvis position, the abdomen opened, and the examination of the annexa proceeds. If free iodine is found in the *cul-de-sac*, the excess is sponged away. Both tubes are separated and examined, and a decision is reached as to the propriety of

saving one or both of them. If even one ovary and half a tube can be retained, it is the rule to save them. The same syringe and the same or one-half strength of the tincture of iodine is then used to strongly distend the tubes with the intention of applying the iodine over the mucosa of the isthmus, if one has been unable to force the fluid into the tube from the uterus. After the irrigation of the tubes, any method of surgically conservative treatment may be practised.

The recovery of patients after this treatment is in no way unlike the usual smooth or even course which characterizes good gynecological surgery. Pregnancy occurred in 2 patients who had pus tubes treated in this manner, and a great many others are living in good health who would formerly have had both annexa removed. I. S. Stone (Va. Med. Semi-Monthly, June 7, 1912).

A 3.5 per cent. solution of iodine crystals in 95 per cent. alcohol is the weakest absolutely reliable preparation of iodine. The author recommends its use in **acute infections of the vulva, vagina, urethra, and the whole of the endometrium; acute peritoneal infections** with proper limitations; chronic conditions following infections of these structures and of the tubes, ovaries, and pelvic peritoneum; in **pelvic surgery** requiring examinations, manipulations, or operations on or through the vagina; such procedures as require opening the cervical canal or uterine cavity from either the vaginal or peritoneal side; as a routine method of preparation of the field of operation on all these structures, as well as the rectum. Iodine requires a maximum of two minutes to prepare the field of operation. J. W. Bovée (Amer. Jour. of Obstet., Feb., 1913).

In various forms of **endometritis** tincture of iodine has been applied to the uterine cavity. According to Reynès, iodine fumigations give excellent results in **ulcerative cervicitis**

and **granulomatous** or **postabortive metritis**, and are also useful in the palliative treatment of **uterine cancer**, after the superficial layers of the tumor have been scraped away. After careful swabbing the vagina and cervix this observer introduces into the former a small pledget of cotton-wool dipped in iodoform, which has been passed in the flame of an alcohol lamp, candle or match. The combustion of the cotton-wool sets the iodine free, its vapors filling the vagina previously dilated with a speculum.

Iodine is especially useful as an intra-uterine injection in **puerperal sepsis**: Iodine, 3 parts; potassium iodide, 6 parts; distilled water, to 1000 parts. When injections are not effectual, the author advocates curettage, after which the uterus is swabbed out with a bit of cotton, previously dipped in tincture of iodine. L. Ammond (*Jour. de méd. et de chir. prat.*, No. 16, p. 625, 1904).

Always use the tincture in full strength on all mucous membrane where inflammation is due to infection. All such cases should be drained with gauze. Whenever iodine in any strength is used in closed cavities, such as the urinary bladder or uterus, either thoroughly douche with saline solution and hydrogen peroxide or insert a drain—preferably a small gauze drain. Do not use a hypertonic salt solution, Wright's solution, or hydrogen peroxide for twelve to twenty-four hours after using iodine. Never use the full strength in the vagina or rectum. In all **indolent wounds** or **ulcers**, apply a bandage as nearly air-tight as possible for twelve to twenty-four hours after a thorough application of iodine. F. E. Walker (*Jour. Minn. State Med. Assoc.*, Feb. 15, 1911).

Louge's method of generating nascent iodine applied to gynecological lesions. The simplest technique for this is to dip a wad of cotton, held

with forceps, into iodoform and take up as much as it will readily hold. The cotton is then lighted and, as soon as the iodoform has burned away the tampon, sending out the amethyst vapors, is pushed deep into the vagina and held in place with a gauze or cotton plug. Or the vapors can be applied through a tube. The procedure is repeated twice a week. Reynès (*Revue prat. d'obstét. et de gynéc.*, May, 1912).

Discussion of a method consisting in the heating of iodoform contained in a flask and the conduction of the iodine vapor generated through a glass tube, the distal end of which is drawn out to a fine point, and which is applied to the cavity or surface to be treated. This method is of particular value in the treatment of **infected wound** and **cavities** that are not readily accessible, including **tuberculous cavities** and **sinuses**, **furuncles** that have been incised, **boils**, and **chronic suppurations** of the **ear** or **mastoid**. It is also of value in **simple metritis**, **inoperable cancer**, and **puerperal infection**. In the last condition the iodine vapor is introduced into the uterine cavity by means of a double-current glass sound (iodine attacks metal). **Vari-cose ulcers** and **soft** or **hard chancres** are also favorably influenced. The duration of the individual treatment is three or four minutes. Louge has proposed the employment of this method in the treatment of **synovitis**, the vapor being introduced into the joint cavity by means of a syringe after the fluid has been evacuated. Boissart (*Gaz. des praticiens; Charlotte Med. Jour.*, July, 1913).

In **colitis** and **dysentery**, ulcerative processes present may be favorably influenced by the introduction, after careful cleansing of the bowel by means of an enema, of 1 pint (500 c.c.) of lukewarm water to which has been added 1 fluidram (4 c.c.) of Lugol's solution. If pain is caused by this mixture, 1 dram (4 Gm.) of

potassium iodide may be substituted for the Lugol solution, or a little extract of opium added.

Maberly has advised internal use of iodine in **phenol poisoning**, non-toxic phenol iodide being formed; also locally, to check phenol corrosion.

Parenchymatous injections of iodine are still employed in **hydrocele** after evacuation of the fluid, the iodine being intended to excite local inflammation, with resulting obliteration of the cavity. It has also been injected in **spina bifida**, with varying results, is not infrequently introduced into **ovarian tumors** after their evacuation, and when injected to the amount of a few minims in **enlarged tonsils** has been observed to induce resolution. **Hydatid cysts** can be treated advantageously in the same way.

Potassium iodide is credited with being an **anti-galactagogue**.

For diagnostic and sometimes also for therapeutic purposes, *injections of iodized oils*, such as lipiodol and iodipin, have come into use since 1921, when Sicard and Forestier first injected lipiodol into the spinal canal for demonstrating and locating with the X-ray obstructions of the spinal canal. It was later used successfully in a similar manner for locating bronchiectases, fistulous tracts and lung cavities, and has been introduced by others for roentgenography of the pericardium, subphrenic cysts, lung abscesses, the stenotic larynx, bronchial displacements, interlobular and intrapulmonary effusions, the vasa deferentia and seminal vesicles, etc.

In spinal localization usually 2 or 3 c.c. of the iodized oil are introduced into the cisterna magna, whereupon the oil descends and is checked at the level of the spinal obstruction. For the bronchial tree, in respect of which

the method has been elaborated to the greatest extent, from 10 to 20 or even 40 c.c. of the oil are introduced by one of several methods, *viz.*, the supraglottic (injection from a cannula held over the glottis); the transglottic (tip of cannula passed through the larynx into the trachea); the subglottic (needle passed into trachea through the cricothyroid membrane), or the bronchoscopic (introduction through the bronchoscope). The distribution of the oil is determined by gravity, and is therefore controllable by posture. Absorption of the oil, which is practically non-irritating, is extremely slow, thus affording an opportunity for treatment by gradual liberation of iodine in the tissues.

In 5 cases of hydropneumothorax and 1 each of pyopneumothorax, purulent pericarditis and peritonitis, all tuberculous, the writers made direct injections of iodized oil, consisting first of 5 c.c. (80 minims) of a light lipiodol, containing 0.11 Gm. of iodine per c.c., then an equal quantity of a 0.44 Gm. lipiodol. The injections were sometimes repeated 3 or 4 times at 15- to 20- day intervals. They proved of diagnostic utility and, except in large effusions, also of therapeutic service, particularly in the case of pericarditis, in which clinical improvement and temporary subsidence of the effusion resulted. The procedure is contraindicated in progressive lung tuberculosis, apparently hastening the morbid process. N. Fiessinger and A. Lemaire (*Presse méd.*, Feb. 17, 1926).

C. E. DE M. SAJOUS

AND

L. T. DE M. SAJOUS,
Philadelphia.

IODOFORM.—Iodoform (*iodoformum*, U. S. P.), though spoken of by Sérullas in 1822, was first used in practice by Bouchardat in 1836. Rhigini, in 1853, brought to light its great

value as an antiseptic and as a disinfectant.

Iodoform is obtained by warming ethyl alcohol, aldehyde, acetone, or certain other organic substances with iodine and potassium hydroxide or carbonate. Its chemical composition is CHI_3 (tri-iodomethane), and it occurs in yellow crystals having a penetrating, persistent, saffron-like odor, which adheres to every object with which the drug comes into contact. This peculiar odor is one of the chief drawbacks in the use of iodoform and has greatly contributed to limit its employment.

Numerous methods for the deodorization of iodoform without impairing its therapeutic properties have been recommended, none, however, with complete success. Probably the best procedure is to mix with it cumarin, an odoriferous principle obtained from the Tonka bean—the fruit of a plant (*Dipterix odorata*) growing in Guiana. Other methods of deodorization consist in the addition of 4 drops of oil of sassafras to the ounce of iodoform (Dodsley); a few drops of oil of bitter almonds or a little musk or tar (Charteris); 1 part each of menthol and oil of lavender to 20 parts of iodoform (Cantrelli), or 1 or 2 parts of creolin to 100 parts of iodoform (von Jaksch).

To remove the odor of iodoform from the clothes or hands, washing in an aqueous solution of tannic acid is an effectual procedure. Ether or chloroform may also be used, or vinegar may be applied freely to the hands after they have been cleansed with soap and water (Ricketts). Constan states that washing the hands with orange-flower water is sufficient to dispel the odor.

Various more or less odorless substitutes for iodoform, some containing the latter in combination with other substances (vioform, iodoformogen) and others of entirely different composition (iodol, eucrophen, aristol, airol), have been introduced.

PREPARATIONS AND DOSE.—

Iodoformum, U. S. P. (iodoform), occurring in a fine, lemon-yellow powder or in crystals, with a peculiar odor and a slightly sweetish, iodine-like taste, is soluble in 9391 parts of water, in 46.7 parts of cold alcohol, in 12 parts of boiling alcohol, in 5.2 parts of ether, and dissolves also in chloroform, benzoin, and fixed and volatile oils. Iodoform is somewhat volatile, and when placed in boiling water vaporizes with the steam. It melts to form a brown liquid at 115°C . and at higher temperatures gives off vapors of iodine. Iodoform or its solutions should be kept in well-stoppered bottles in a dark and cool place. Dose, 1 to 5 grains (0.06 to 0.3 Gm.).

Unguentum iodoformi, U. S. P. (iodoform ointment), is made by triturating 1 part of iodoform with 7 parts of melted petrolatum and incorporating 2 parts of wool fat.

The following unofficial preparations also contain iodoform:

Iodoformum aromatisatum, N. F. IV ("deodorized" iodoform), consists of iodoform with admixture of 4 per cent. of cumarin.

Pulvis iodoformi compositus, N. F. III (compound iodoform powder; naphthalene iodoform), is a mixture of 20 parts of iodoform with 30 parts of boric acid, 50 parts of naphthalene, and 2.5 parts of oil of bergamot. Used externally.

Collodium iodoformatum, N. F. III (iodoform collodion), consists of

flexible collodion in which 5 per cent. of iodoform has been dissolved.

Iodoformogen (iodoformalbumin), a nearly odorless mixture of iodoform and albumin, occurs as a fine, bulky, light-yellow powder, containing about 12 per cent. of iodine. It is insoluble in water, and can be sterilized at the boiling point of water without decomposition. Iodoform is slowly freed from the mixture when it is placed on an open tissue surface. Used externally as dusting powder.

In the local use of iodoform the powdered drug should be applied directly to the base of ulcerations and not on the surrounding skin, the object being to restrict the amount of the drug used to that which is actually necessary, in order to minimize the chances of serious iodine poisoning. Iodoform should not be sterilized by heat, but by means of mercury bichloride in 1:1000 solution. Solutions of iodoform should be kept in colorless glass bottles, to prevent iodine liberation under the influence of light. Saturated solutions of iodoform in ether, which are very unstable, readily assuming a reddish color, may be rendered more stable by the addition of alcohol as well as by protection from light. Alcohol saturated with camphor dissolves eight times as much iodoform as pure alcohol.

CONTRAINDICATIONS.—Symptoms of mercurial intoxication may result from the simultaneous use of iodoform externally and calomel or other mercurials in ordinary doses internally. Some caution is therefore necessary in the combined administration of these remedies. Some degree of danger also attends the simultaneous use of iodoform and phenol.

Iodoform had best be avoided in cases with an idiosyncrasy to iodine or iodides.

PHYSIOLOGICAL ACTION.—

Although containing about 29 parts by weight of pure iodine in 30, iodoform is rendered almost non-irritant by the combination of the carbon and hydrogen it contains with the iodine, although in a few cases with special local sensitiveness it causes evidences of irritation in the vicinity of wounds over which it has been placed. It exerts a noticeable local anesthetic action when freely applied.

Iodoform is not germicidal *per se*, but when brought into contact with moist tissue surfaces is believed to give off iodine, which is the true origin of its apparent antiseptic virtues. Iodalbuminates and di-iododi-acetylene are considered to be products of the decomposition of iodoform when placed upon the living tissues.

The general effects of iodoform, upon absorption into the system, are practically those of iodine and the iodides (*q.v.*). Indeed, iodine split off from iodoform in the presence of alkalies and of proteins forms alkaline iodides and iodalbuminates with these two classes of substances, and, being thus absorbed in the same form as is iodine, acts like the latter. It is believed by some, however, that iodoform may in part reach the blood without change and give rise directly to the cerebral symptoms sometimes seen in iodoform poisoning.

It is considered possible by many observers that in iodoform poisoning cardiac acceleration may be a result of abnormal activity of the thyroid gland brought on through the presence of additional iodine. It has been shown that iodoform may consider-

ably augment the thyroid secretion. After the absorption of iodoform, iodine may be demonstrated in small amount in the saliva, bronchial secretion, and sweat. As shown by Rummo, the elimination from the system of the iodides formed from iodoform takes place slowly, though it begins promptly after the absorption of the drug. Iodides have been detected in the urine for over a month after the absorption of iodoform.

UNTOWARD EFFECTS AND POISONING.—The local untoward effects of iodoform consist generally of an erythematous eruption. After a period of apparent perfect tolerance the wound becomes surrounded by an inflammatory area, at the circumference of which vesicles may form ("iodoformic herpes"). Petechiæ may also develop. If the use of the drug is persisted in, the lymphangitis spreads, pain is experienced locally, and signs of general intoxication appear.

Experiments in animals have shown that when used in the peritoneal cavity iodoform awakens an inflammatory process which results in an excessive formation of adhesions.

General toxic symptoms may follow the external use of iodoform without any preceding local symptoms, or may result from its use by mouth.

The usual clinical signs of systemic poisoning are, according to Chéron, a sudden rise of temperature to 102.2° or 104° F. and the appearance on the same or the following day of a skin eruption, often of an erythematous or scarlatiniform type. Itching may be present, and an eczematous type of eruption has also been reported. Anorexia, nausea, and

vomiting may appear with the eruption, or exist alone.

Another characteristic manifestation is cerebral excitement, expressed in restlessness and sleeplessness, or even actual delirium. Violent headache and giddiness may be experienced, and the taste and odor of iodoform may be noticed. The pupils are occasionally dilated, but oftener contracted and motionless (McLean). The pulse usually shows a decided increase in rate, which may soon attain 135 to 150 per minute, and is rather small and wiry. With the general discomfort experienced sometimes becomes associated mental depression, which may deepen into melancholia with hallucinations and illusions of persecution. Where this condition is marked, a period of violent mania lasting some hours or days is apt to follow. Collapse and death may occur, or permanent insanity may supervene. No other poison, according to Cushny, produces these cerebral symptoms in so marked a manner as iodoform, and no similar action has been noted in experiments on animals.

In the "syncopal or asthenic form" of iodoform poisoning (McLean) the patient is overcome with dizziness, mental confusion, and pronounced lethargy. The pulse becomes weak and rapid. Sphincter paralyseis may be observed, and sudden death from heart-failure sometimes follows.

Report of a case of iodoform poisoning in a man 30 years of age after a third injection of 100 c.c. (3½ ounces) of a 10 per cent. iodoform-glycerin emulsion into a psoas abscess. The symptoms were as follows: Slight vomiting during the first day after the injections, a progressive somnolence beginning on

the ninth day, a widely disseminated acneiform eruption, desquamation of the buccal mucous membrane, crust formation in the nose, agglutination of the eyelids, followed by an increase in the reflexes of the lower extremities and stertorous respiration. Large quantities of iodoform were found in the urine. In spite of the evacuation of the iodoform emulsion by means of saline irrigation, death followed after two days. The author considered the cause of this rare symptom-complex to be the caseation of both suprarenal capsules, which was found *post mortem*. There had been no symptoms of Addison's disease. Anschutz (*Beiträge z. klin. Chir.*, Bd. xxviii, H. 1, S. 233, 1901).

The more common cutaneous conditions resulting from iodoform are general redness and swelling of the skin of the abdomen and down the thighs, sometimes extending from the trunk to the upper extremities. In several cases it has been associated with a fine, vesicular eruption, principally affecting the region of the wound. Other observers have had cases in which the vesiculation has extended into the deeper layers of the skin, resulting in considerable edema and in some instances in a sanguinolent effusion resembling superficial gangrene. The writer reports a case peculiar in that large blebs, somewhat like those of pemphigus, appeared in the neighborhood of the incision. He advises inquiry, in any abdominal or pelvic operation in which iodoform is likely to be used, whether the patient has been subject to any cutaneous affection, and, if so, to substitute another dressing for that of iodoform. McNaughton-Jones (*Medical Press*, Feb. 24, 1904).

The quantity of iodoform capable of causing death has been estimated at 1 dram, according to a case observed by Langenstein, but from other evidence it seems probable that in the majority of cases this dose

would not prove fatal. Although Czerny has reported a death after ingestion of 1½ drams, Frauenthal records the case of a woman who took 2 drams at once, with severe headache, abdominal cramps, and purging as the only resulting effects.

Fatty changes in the liver, kidneys, heart, and muscles are likely to be found after lethal iodoform poisoning. Evidences of marked gastrointestinal irritation, with degeneration of the epithelium, and extravasations of blood in the kidneys and under the endocardium may be noted. In cases of protracted iodoform intoxication in animals Koriandère noted also extreme emaciation, anemia, purulent bronchitis, rhinitis, and conjunctivitis, and an accumulation of pigment in the Malpighian bodies. Terson reported the case of a woman who, having sustained injuries of the thighs and abdomen to which iodoform dressings were applied, developed after three weeks a progressive amblyopia, accompanied by atrophy of the temporal halves of both disks.

Report of the case of a patient to whom there had been twice administered, after puncture of a psoas abscess, injections of 10 per cent. iodoform-glycerin, 300 Gm. (10 ounces) in all of this preparation having been used. Twenty-five days after the first injection and four days after the second the patient's sight became hazy, and four days later he was unable to read or write. Examination of the eye showed no change. After three weeks, improvement set in and normal vision was regained two weeks later. The case was one of toxic amblyopia, ascribable to a retrobulbar neuritis. A. Sarasoff (*Wiener klin. Woch.*, No. 47, 1907).

Some of the untoward results observed from the use of iodoform have been due to impurities. A practical

procedure for testing the purity of iodoform is to shake some of it up with distilled water, filter, and treat the liquid with an alcoholized solution of silver nitrate. If in twenty-four hours no precipitation occurs, or only a slight grayish cloudiness develops, the drug may be deemed pure.

The *diagnosis* of iodoform poisoning may be facilitated by estimating the amount of iodine which is being eliminated in the urine, as follows: A small pinch of powdered calomel is placed upon a saucer, and a few drops of the urine placed upon it. The urine and calomel are then mixed together with a glass rod. If the urine contains a notable amount of iodine there will be noticed a well-marked yellow coloration, indicating that the iodoform is being absorbed to a dangerous extent.

Treatment of Iodoform Poisoning.

—Immediate removal of the drug from the surface in cases of intoxication from surgical dressings is obviously indicated. This can readily be done by means of a **warm solution of starch**, which will take up all the free iodine present. **Alcohol** or **hot water** may be used instead. According to F. E. Miller, a weak alkaline solution of **magnesia, sodium bicarbonate, lime water, Burow's solution** (1 to 4), or **ichthyol** (1 to 10) is useful for local application in cases of unsuspected idiosyncrasy to iodoform. Internally, 1 dram (4 c.c.) of **milk of magnesia** should be given every three hours until the bowels move, and care taken on succeeding days to keep the intestines active. In fully established cases of iodoform poisoning **potassium bromide** may be given internally to assist in counteracting the poisonous effects.

When a toxic dose of iodoform has been taken internally, the stomach should be emptied and 20 grains (1.3 Gm.) of potassium bromide given in a half-tumblerful of water. Four 10-grain (0.65 Gm.) doses should then follow at hourly intervals. The bromide not only antagonizes the cerebral excitant effects of iodoform, but is considered by some to act as a solvent and eliminant with regard to the former drug. It seems not unreasonable to suggest that, just as bromides tend to a certain extent to take the place of chlorides in the body when taken repeatedly and promote the elimination of chlorides in the urine, they may displace iodine-containing compounds from the body fluids and prevent their action.

Case of an infant for whom, after a circumcision which did not heal satisfactorily, an iodoform salve was ordered. The day after its first application the child was somnolent, with shallow breathing, and refused the breast. There was cyanosis, retraction of the epigastrium, and laryngeal spasm. The pupils were contracted to the size of pinpoints. The circumcision wound had not yet healed, but a severe eczema had been set up involving the scrotum and the inner surface of both thighs. The temperature was 100° F. (37.8° C.) and the heart's action feeble. A **hot enema** was administered with a bath, and **frictions with alcohol and mustard**. One-minim (0.06 c.c.) doses of tincture of **belladonna** were given every hour. The following morning the child was in a normal condition. The eczema rapidly improved. The writer especially directs attention to the apparent antidotal action of the belladonna. J. C. Josephson (*Med. Record*, April 14, 1900).

THERAPEUTICS.—Iodoform is not now used in surgery as much as in the last decade of the nineteenth

century, both its unpleasant odor and occasional inefficiency having been factors in causing its partial abandonment. Decomposition of the drug in contact with the tissues, with liberation of iodine, appears to be essential to its antiseptic action, and such decomposition is variable, sometimes being so slight as to preclude appreciable antiseptis, while at others it may be so pronounced as to result in iodism. Experiments with infected wounds in animals leave doubt as to the activity of iodoform. Lomry observed that, if wounds inflicted on dogs or guinea-pigs were infected with staphylococci or streptococci and then treated with iodoform, they healed more quickly and secreted less than those not thus treated. Fraenkel, on the other hand, found that iodoform caused the formation of giant cells, and that its use resulted in more exudation and more connective-tissue production than the use of other antiseptic powders, and, therefore, concluded that it was often harmful in abdominal wounds. In tuberculous conditions, on the contrary, according to this author, iodoform is useful because of this same property of favoring fibrosis—a property, by the way, which Cornil and Cowdray had already noticed and written of in 1900.

It is in the treatment of "surgical" tuberculous conditions that iodoform now finds one of its chief applications. Among the conditions that may be advantageously treated with it are **tuberculous abscesses** and **sinuses**, including those of joint and **bone tuberculosis**; **tuberculous adenitis**, and **tuberculous pleurisy**. In joint tuberculosis injections of a 10 per cent. suspension of iodoform in sterile

olive oil are employed. Freeman's directions for the application of this treatment may be summarized as follows: Absolute cleanliness should be observed. The iodoform should be soaked for twenty-four hours in a 1 to 1000 solution of bichloride of mercury, stirred occasionally with a glass rod to make sure that the solution touches every particle of the powder. It is next filtered, employing a filter-paper through which has been poured a quantity of boiling water. The remainder of the bichloride is then washed away with sterile water. The iodoform is removed from the filter with a surgically clean knife and rubbed up with the oil in a sterile mortar, about 4 per cent. going into solution and 6 per cent. remaining in suspension. The oil is best rendered germ-free by keeping it at the boiling-point for about half an hour. (If the mixture is kept in a dark place in a sterilized bottle stopped with germ-free cotton, it will not deteriorate for a long time.) The injections should be made both into the joint cavity and into the surrounding infected tissues. It is best to but partially withdraw the needle and insert it in a new place, rather than to make a number of punctures in the skin. If tuberculous pus is present, it should first be withdrawn. One syringeful of a 10 per cent. suspension of iodoform is an average dose. It is well to begin with a moderate quantity and watch carefully for symptoms of iodoform poisoning—which, however, seldom appear. In general, the injections can be repeated every two or three days over a period of several weeks, and then continued at intervals of a week or two.

Lucy gives the following formula

for an iodoform emulsion for injection in **tuberculous sinuses**: Iodoform, 3 parts; starch, 1 part; mix until a fine powder is obtained and add glycerin, 20 parts, and water, 12 parts. Heat gradually, stirring the mixture constantly, up to 271.4° F.

To avoid secondary infection in the treatment of **tuberculous abscesses**, Wederhake punctures with a large cannula, aspirates the pus, and injects 10 per cent. iodoform-glycerin. This is repeated after 3 days. A 5 per cent. solution of tannic acid, 1 to 5 c.c. (16 to 80 minims) according to the size of the abscess cavity, is then injected without placing the abscess wall under tension. This hardens most of the pus into a mass, and 2 hours after the injection a small incision is made in the abscess and the latter emptied by gentle pressure. A dressing of iodoform and tannic acid solution is then applied. K. Keilmann (Klin. Woch., May 27, 1924).

In **tuberculous laryngitis** the local use of iodoform has been followed by good results. The ulcerated surfaces having been carefully cleared of their mucopurulent discharges by a detergent spray, a solution of iodoform in ether may be directly applied at short intervals or likewise used as a spray. If very finely powdered it may be applied by means of an insufflator, to relieve the local discomfort and hoarseness.

In operations on the parietes of the mouth or pharynx, *e.g.*, in excision of the maxilla, von Bergmann highly recommends tight packing of any cavities or open wounds remaining with iodoform gauze. After 159 operations of resection or excision of the tongue performed by this surgeon, with iodoform gauze packing of the wound, not one patient died from local infection. The value of

iodoform gauze for plugging the wound after rectal operations is well known. A 5-grain (0.3 Gm.) suppository of iodoform is useful in **tuberculous disease of the rectum and rectal fissures**. Where dryness of the parts is required for prolonged periods, iodoform gauze is particularly desirable.

The Mosetig-Moorhof bone-wax, employed for filling aseptic cavities in bones, consists of iodoform, 60 parts; spermaceti and oil of sesame, of each, 40 parts. For information concerning its use the reader is referred to the article on **BONES, DISEASES OF**.

Good results obtained in all kinds of **acute and chronic abscesses, tuberculous peritonitis, phlegmons, mastitis**, and various medical affections with effusion, by the use of a mixture of 1 part of iodoform with 10 parts of glycerin, which the author injects through a large puncture needle after withdrawing part or all of the contents of the abscess or other process. He never found it necessary to make more than three or four injections; one was generally sufficient. The method also proved effective in **inflammatory processes in the knee, acute peritonitis, polyserositis, and pleurisy with effusion**. Vandini (Gaz. degli Ospedali, Feb. 8, 1910).

Excellent results have in recent years been obtained in **suppurative otitis media**, disease of the **nasal accessory sinuses**, and **follicular tonsillitis** by treatment with iodine vapor set free from iodoform by the application of heat. The iodine is thus not only applied in a highly penetrating form, but probably in a nascent state, which renders it powerfully effective as an antiseptic. As suggested by F. E. Miller, the iodine vapor can be applied with a De Vilbiss metal-

tipped insufflator by heating the flexible tip for seven seconds in an alcohol or Bunsen flame; as soon as the preliminary reddish-blue vapor passes off and a greenish fluorescence appears, the insufflation should be begun. The degree of heat of the vapor can easily be tested by holding the nozzle 1 inch from the tip of the operator's tongue; a pleasant warmth and taste indicates a correct condition of the vapor for application. In the case of the ear, *e.g.*, the vapor can be blown steadily into either portal of the middle ear for about three seconds, causing a pleasant heat and soothing sensation for ten minutes thereafter, besides the therapeutic effect. According to Miller, nebulization of 3 drops of 1:1000 epinephrin hydrochloride solution in the ear previous to the vapor insufflation adds to the efficiency of the latter.

The fumes set free upon heating iodoform are less irritating than those liberated from pure iodine, as they do not tend at once to deposit in irritating crystalline particles. In treating the bladder with these fumes this organ should first be emptied through a catheter and its capacity carefully noted by introducing tepid sterile water. The apparatus used consists of a small bulb, heated by an alcohol lamp, and with which is connected a large, graduated hand syringe, for blowing out the vapor. First 0.05 to 0.1 Gm. ($\frac{1}{2}$ to $1\frac{1}{2}$ grains) of iodoform is placed in the bulb and the catheter adapted to an outlet from the latter. When, upon heating the bulb, violet fumes appear, the syringe is gradually emptied to an extent sufficient to fill the bladder, the capacity of which was previously ascertained. The rubber tube is then closed off, to prevent reflux of vapor into the apparatus, and the fumes allowed to act a few minutes (three, on an average) according to

individual tolerance, after which the bulb is detached from the catheter and, after the bladder has emptied itself, the catheter withdrawn. The same or even simpler apparatus may be used in treating affections of the external or middle ear, nasal cavities, or pharynx.

For intrauterine treatment, the vagina, cervix, and endometrium should first be dried, and a non-fenestrated rubber drain, sufficiently small to permit of escape of the fumes between it and the walls of the cervical canal, inserted into the uterine cavity, into which the vapor is then passed. The cervix and vagina may with advantage be given the treatment at the same sitting, after the endometrium.

Wounds can be treated by igniting and at once blowing out a pledget of cotton previously fixed to the end of a glass rod and rubbed lightly in iodoform. Very small areas can be given strictly local treatment by projecting the fumes on them from the small end of a funnel. In **boils** the Bier method and iodine treatment can be combined by the use of a cup filled with the iodine vapor. For the tincture of iodine local treatment in **erysipelas** and **variola**, iodine vaporization can, furthermore, be advantageously substituted.

Glass apparatus stained by the products of iodoform decomposition can be easily cleansed by means of concentrated sulphuric acid to which has been added a little chromic acid, potassium dichromate, or potassium permanganate. G. Meillère (*Tribune méd.*, March, 1913).

Iodine vapor can readily be set free from iodoform by heating the latter with the electric cautery. The author has had constructed a simple insufflator consisting of a small glass bottle, a rubber bulb and tube, and an ordinary electrocautery, the platinum extremity of the latter dipping down to the bottom of the bottle, while a convenient handle is attached to its other extremity. The whole apparatus, which is rather

light, is held by the operator by this handle, his other hand (or an assistant) manipulating the rubber bulb. The outlet for the iodine vapor is conical, so that a number of differently shaped and curved attachments can readily be adapted to it. Metallic parts are reduced to a minimum to avoid oxidation, even the conical outlet being of hard rubber.

With this apparatus excellent curative results can be obtained in a variety of conditions. In **follicular tonsillitis** insufflation of a little nascent iodine vapor into the crypts through a small curved tube causes prompt recovery. After a few insufflations the crypts are completely disinfected and tend to become smaller. The entire tonsil atrophies rather easily, the necessity for its surgical removal being thereby obviated. In **maxillary or frontal sinusitis**, after either catheterization through the natural channels, intranasal puncture, or alveolar penetration, the surfaces in these sinuses can readily be covered with a deposit of iodine through an antral or frontal cannula adapted to the iodoform bottle. The fungous covering of the lining membrane subsides and the odor disappears, generally after the very first sitting. In **polypoid ethmoiditis** the iodine vapor is insufflated at the middle meatus.

Suppurative otitis media, especially in its chronic form, is greatly benefited by the treatment. With a small catheter, shaped like Hartman's cannula for irrigation of the attic, the iodine vapor can readily be introduced even into the mastoid antrum.

In **ozena** the treatment causes the odor rapidly to disappear, the secretions to become fluid, and the mucous membrane to return to its normal color. Where the membrane is in an advanced state of atrophy and paraffin injections are no longer borne, the introduction of nascent iodine vapor causes a more rapid improvement than any other measure.

The author reports two illustrative cases of obstinate **maxillary sinusitis**

and **otorrhea**, respectively, in which iodine vapor brought about prompt curative results—immediate deodorization and almost immediate arrest of secretion—where the ordinary procedures had failed. A. Maurice (Arch. gén. de méd., Feb., 1914).

Treatment with nascent iodine fumes is indicated in all primary or secondary **tuberculous bladder affections**, except during acute exacerbations. The method is superior to all others for this purpose; it improves, soothes, and seems harmless. The capacity of the bladder increased in about 50 per cent. of the cases, though the incontinence did not show any improvement. In the majority of the cases the benefit was prompt and striking. The bladder need not be rinsed out beforehand unless it is much contaminated, and only plain boiled water should be used. About 0.05 or 0.1 Gm. ($\frac{3}{4}$ to $1\frac{1}{2}$ grains) of the iodoform is gently heated, and when the violet fumes issue from the tip of the cannula the alcohol lamp is set aside and the fumes are pumped into the bladder, stopping when the patient shows signs of pain or a desire to urinate. The fumes are retained in the bladder for from half a minute to two minutes. The sittings are given once or twice a week. If the iodoform is impure or impaired by exposure to the air or moisture, the nascent iodine vapor is correspondingly unreliable. Normand (Jour. d'urol., March, 1914).

In ophthalmic conditions iodoform is also frequently of value. In **corneal ulcer** it may be dusted on in powder form. In **diphtheritic conjunctivitis** it may be used either as powder or in an ointment. In **catarrhal dacryocystitis** iodoform has been recommended for promoting local healing. Haab has even advised the introduction of small sterile rods of iodoform into the anterior chamber of the eye in beginning infection of

this chamber from the penetration of **foreign bodies** and in suppuration of the corneoscleral junction after **cataract extraction**.

In gynecological affections iodoform may be employed in the form of crayons, as an ointment, or in a powder, introduced with an insufflator (Montgomery). Iodine vapor set free from iodoform by heat has also been employed with good results in pelvic infections. In **erosion of the cervix** a saturated solution of iodoform in ether (1 in 6 parts) may be topically applied with advantage. In **vaginitis** the drying properties of iodoform gauze are of decided value.

Among venereal conditions in the male in which iodoform has proven useful is **chancroid**. Applied directly to the bare ulcerations, it usually exerts a decided inhibitory action on bacterial pullulation, though in a few cases irritation and inflammation may result from the drug itself. The objectionable odor can be in part disguised by adding to the iodoform oil of lavender or attar of roses in the proportion of 1 drop to 1 dram (4 Gm.), or finely powdered coffee (1 part in 5). In **chancroidal lymphadenitis** (bubo) which has gone on to pus formation the abscess should be evacuated by puncture and a 10 per cent. iodoform-glycerin emulsion injected and evacuated three times in immediate succession. If a repetition of this procedure is not followed by cessation of pus formation the abscess should be incised, curetted gently, and packed with iodoform gauze.

Similar treatment is indicated in **suppurative gonococcal** or, more rarely, **sypilitic lymphadenitis**.

Internal use of iodoform has never

received much support. It has been tried by many in **pulmonary tuberculosis**, but the results have generally been disappointing, although Gosse's experiments showed that guinea-pigs whose system was kept saturated with iodoform could stand inoculation with tuberculous material with impunity. Likewise in **sypilis** the effects of iodoform taken internally have not, as a rule, been satisfactory.

C. E. DE M. SAJOUS

AND

L. T. DE M. SAJOUS,
Philadelphia.

IPECAC.—Ipecac (ipecacuanha) is the root of the *Cephaelis Ipecacuanha* (Rio or Brazilian ipecac) or of *Cephaelis acuminata* (Cartagena or Panama ipecac), of the family *Rubiaceæ*. Ipecacuanha contains three alkaloids, *emetine*, *cephaeline*, *psychotrine*; a glucosid called ipecacuanhic acid, which resembles quinic and caffe-tannic acids; gum, resin, starch, a volatile oil, lignin, and sugar. The powdered root has a slight, but characteristic, nauseous taste.

The alkaloid emetine is a whitish powder, of a bitter taste, and darkening upon exposure. It is soluble in alcohol and chloroform, slightly soluble in ether, and very slightly soluble in water. It is present in the root in a proportion of somewhat less than 1 per cent. Emetine forms halogen salts and a nitrate, the acetate and sulphate being amorphous.

Cephaeline occurs as snow-white, fine, interlacing needles, which rapidly turn yellow. It is soluble in alcohol, chloroform, benzin, and slightly soluble in ether, but more soluble in boiling petroleum ether than emetine, and may be readily separated from

the latter by its solubility in sodium hydroxide solution. Its salts are amorphous.

Psychotrine is an uncrystallized alkaloid which is decomposed by light and of but little therapeutic value.

From an analysis of 145 different lots and samples of ipecac, representing in all many thousands of pounds of drug, the authors' records show that commercial ipecac averages 2.17 per cent. of total alkaloids. The average amount of emetine is to that of cephalin as 63 is to 37. There is little or no difference in alkaloidal strength between Rio and Cartagena ipecac. Walters and Koch (Jour. Pharm. and Exper. Therap., July, 1917).

PREPARATIONS AND DOSE.—

Ipecacuanha, U. S. P. (ipecac), the dried root of ipecac, required to contain not less than 1.75 per cent. of ether-soluble alkaloids. Dose, as expectorant, 1 grain (0.06 Gm.); as emetic, 15 to 30 grains (1 to 2 Gm.); in dysentery, 30 to 60 grains (2 to 4 Gm.).

Fluidextractum ipecacuanhæ, U. S. P. (fluidextract of ipecac), required to contain 1.35 to 1.65 Gm. of ether-soluble alkaloids per 100 c.c. Dose, as expectorant, 1 minim (0.06 c.c.); as emetic, 15 to 30 minims (1 to 2 c.c.).

Syrupus ipecacuanhæ, U. S. P. (syrup of ipecac). 100 parts of which are made from 7 parts of fluidextract of ipecac, 10 parts of glycerin, and syrup, a sufficient quantity to make 100 parts by volume. Dose, as expectorant, 5 to 20 minims (0.3 to 1.3 c.c.); as emetic, 2 to 8 fluidrams (8 to 30 c.c.).

Pulvis ipecacuanhæ et opii, U. S. P. (powder of ipecac and opium; Dover's powder), containing 10 per cent. each of ipecac and powdered opium and

80 per cent. of lactose. Dose, 5 to 15 grains (0.3 to 1 Gm.).

Tinctura ipecacuanhæ, N. F. (tincture of ipecac, replacing Vinum ipecacuanhæ, N. F. IV), containing 10 per cent. of fluidextract of ipecac and 20 per cent. of alcohol. Dose, as expectorant, 5 to 15 minims (0.3 to 1 c.c.); as emetic, 2 to 6 fluidrams (8 to 24 c.c.).

Tinctura ipecacuanhæ et opii, N. F. (tincture of ipecac and opium), representing the tincture of opium, full strength (evaporated down), with 10 per cent. fluidextract of ipecac. Dose, 5 to 15 minims (0.3 to 1 c.c.).

Syrupus ipecacuanhæ et opii, N. F. (syrup of ipecac and opium), each fluidram (4 c.c.) of which represents 5 minims (0.3 c.c.) of the preceding tincture. Dose, 1 fluidram (4 c.c.).

Emetine hydrochloridum, U. S. P. (emetine hydrochloride), occurring as a white or slightly yellowish crystalline powder, odorless, gradually darkening on exposure to light, and freely soluble in water or alcohol. It contains variable amounts of water of crystallization. Its solution is slightly acid to litmus. Dose, $\frac{1}{4}$ to $\frac{3}{4}$ grain (0.015 to 0.045 Gm.).

Emetine bismuth iodide, unofficial, contains about 20 per cent. of emetine and occurs as an orange-yellow powder, with a somewhat bitter taste, slightly soluble in water or diluted acid. Dose, $\frac{3}{10}$ grain (0.2 Gm.) daily for 4 days.

PHYSIOLOGICAL ACTION.—

Locally, ipecac, applied to the mucous membranes or skin, acts as an irritant.

It gives rise to a papular eruption, which becomes pustular and proceeds to active ulceration if the application is persisted in.

General Effects.—*Alimentary Tract.*—Internally, small doses of ipecac frequently repeated give rise to nausea and increased flow of salivary, biliary, and bronchial secretions. In persons sensitive to its influence vertigo and flushing may appear in addition.

With large doses these effects are increased in intensity; nausea appears at once and vomiting later occurs, without producing excessive prostration, an excess of the drug being ejected before it has had time to induce marked depression.

These effects are due mainly to the alkaloids contained in ipecac, especially the cephaeline, which has twice the emetic power of emetine. The emesis has generally been ascribed to local irritation of the stomach, but Eggleston and Hatcher in 1915 found that the emetic dose was almost the same upon hypodermic injection as upon introduction in the stomach, and witnessed vomiting movements under ipecac in eviscerated animals. The emesis is thus of central origin, but the local action facilitates the emetic response, since gastric introduction acts more promptly than hypodermic.

The smaller therapeutic doses give rise to customary accompaniments of the nausea, *viz.*, increased perspiration and saliva; augmented flow of mucus, particularly in the respiratory tract; temporary acceleration of the pulse, and general weakness.

Circulation.—Both emetine and cephaeline tend to lower blood-pressure by depressing the heart, but this effect is much less marked upon hypodermic administration than upon intravenous. Both the active alkaloids of ipecac have been observed to constrict the blood-vessels after destruc-

tion of the brain and spinal cord, especially emetine. This vasoconstriction, however, is not effectual in preventing a diminution of blood-pressure during the period of nausea from full therapeutic doses; and where toxic doses are given to animals, the direct cardiac depression is such as likewise to preclude any rise of blood-pressure. The pulmonary system seems to be depleted of its blood, judging from the pallor of the tissues post mortem, an active hyperemia of the gastrointestinal tract apparently compensating for this.

Secretions.—Ipecac tends to increase secretions, especially those of the respiratory tract and skin.

UNTOWARD EFFECTS AND POISONING.—Excessive doses of ipecac produce, if vomiting fails to take place or does not sufficiently remove the drug, the effects of irritant drugs in general, *viz.*, abdominal pain, diarrhea, and bloody stools, followed by collapse. Acute nephritis may occasionally result. Urticaria sometimes follows its internal use.

In the lower animals lethal doses of emetine cause death by paralysis of respiration, the heart continuing to functionate after respiratory movements have ceased. The surface temperature falls, but the internal temperature either remains stationary or exhibits a slight rise, owing to the irritant action of the emetine upon the intestinal mucous membrane (d'Ornellas).

Post-mortem examination of animals killed by emetine reveals considerable gastrointestinal irritation. The lungs are often hyperemic and present patches of hepatization; sometimes, however, they are exsanguinated.

Treatment of Poisoning.—Poisoning by ipecac or its alkaloid, emetine, is uncommon. The indications, where it occurs, are to remove the drug from the stomach, if possible, by means of the **stomach-tube**. **External heat**, with **ammonia**, **strychnine**, and other respiratory stimulants, as well as **digitalis**, should be resorted to.

Ipecac may produce phenomena of intolerance manifested by asthma or eczema. These may be attributed to allergy. In 1 such case, a druggist, ipecac caused dyspnea and asthma and, when injected in small amount, transitory amaurosis, vertigo, a scarlatinoid and urticarial eruption, Raynaud's syndrome and coryza. Another druggist became sensitive to emetine, and gave strongly positive skin tests. **Desensitization** was rapidly obtained by subcutaneous injections of emetine, beginning with 1 c.c. (16 minims) of a 1:10,000 solution and increasing up to 0.05 Gm. ($\frac{3}{4}$ grain) of emetine. Widal, Abrami and Joltrain (*Presse méd.*, Apr. 22, 1922).

THERAPEUTICS.—Ipecac is a safe and efficient emetic. It is free from depressing and irritating effects when given in ordinary doses. On the other hand, it is sometimes slow in its action. Ipecac in emetic doses (4 to 20 grains—0.26 to 1.3 Gm.—of the powder or 1 to 8 fluidrams—4 to 30 c.c.—of the syrup) may be used to empty the stomach in cases of **acute indigestion**, **migraine**, or bilious sick headache. In membranous croup, **bronchial asthma**, **capillary bronchitis**, lodgment of **foreign bodies**, **pertussis**, and in **laryngismus stridulus** it may be employed in emetic doses for its mechanical effects. In the bronchitis of small children, who swallow the mucus coughed up, emetic doses of ipecac will relieve the stomach and improve the condition of the lungs.

As an emetic in cases of poisoning ipecac is inferior to mustard or the sulphate of zinc or copper on account of its less efficient and slower action.

As an antemetic, in small doses— $\frac{1}{10}$ to $\frac{1}{4}$ grain (0.006 to 0.015 Gm.) of the powder every hour—ipecac has seemed of value. It is useful in vomiting of drunkards, of **pregnancy**, of **migraine**, and especially in **nervous vomiting** and the morning vomiting of weakened **convalescents** from acute diseases. In the vomiting of children with **acute catarrhal gastritis** ipecac is also useful. It has a greater influence over the vomiting of children than over that of adults. The vomiting in **cancer of the stomach** may be relieved by ipecac. Small doses— $\frac{1}{10}$ to $\frac{1}{6}$ grain (0.006 to 0.01 Gm.)—are beneficial where **hepatic torpor** and insufficient excretion of bile exist. In flatulent dyspepsia doses of $\frac{1}{10}$ to $\frac{1}{4}$ grain (0.006 to 0.015 Gm.) given after meals are followed by a subsidence of the **flatulence**. One grain (0.06 Gm.) taken fasting every morning will remove **dyspepsia with constipation**, cold extremities, and a feeling of weight in the stomach.

In children with chronic anorexia, poor nutrition, constipation interrupted by attacks of diarrhea, acetone breath, dry and coated tongue, and hard and chalky stools except during diarrhea, when they become mucilaginous, blood-stained and fetid, the writer recommends ipecac in ascending doses, beginning with 1 drop of the tincture in a little sugar and water twice daily $\frac{1}{2}$ to 1 hour before meals, and increasing by 1 drop twice daily each day until 10 to 40 drops in the 24 hours, according to age, are reached. Nausea rarely results. To prolong the effects, Bérard gives decreasing doses after the highest amount has been attained. R. Saint-Philippe (*Pract.*, Aug., 1923).

An ointment of the powder of ipecac (25 per cent.) has been used as counterirritant. In the early stage of **bronchitis**, when the secretion from the lungs is abundant and tenacious, ipecac will do good service in non-emetic doses. Even the inhalation of wine of ipecac in the form of a spray produced by hand atomizer has been recommended in the treatment of **hoarseness**, winter cough, and **bronchial asthma**. For this purpose the wine may be used either pure or diluted with 1 or 2 parts of water. At the first application it sometimes excites a paroxysm of coughing, which generally soon subsides; but should it continue, a weaker solution should be used. As a rule, the patient at first will bear about 20 compressions of the bulb without nausea. The inhalation should be used at first daily, and in bad cases two to four times daily; later, every other day suffices, and the interval may be gradually extended. As the spray is used for its topical effect, the patient is directed to spit out, or even to rinse out, the mouth at each pause in the administration, for a much larger quantity of the wine collects in the mouth than passes into the lungs. In this way vomiting and even nausea are avoided.

In congestion of the lungs following **influenza** Huchard prescribed as follows:—

℞ *Powdered ipecac* gr. iij (0.2 Gm.).
Ergotin ℥ss (2 Gm.).
Brandy f℥x (40 c.c.).
Mucilage of acacia f℥iiiss (100 c.c.).

M. Sig.: One tablespoonful every hour.

In the early stages of **bronchopneumonia** Grasset administers full doses of ipecac in the following form:—

℞ *Powdered ipecac* 3ij (8 Gm.).
Bitter orange-peel ... 3j (4 Gm.).
Water f℥iv (120 c.c.).

Reduce to 3 fluidounces (90 c.c.) by boiling, and add:—

Syrup of orange flowers f℥j (30 c.c.).

Sig.: One teaspoonful every three or four hours.

In **bronchitis**, especially in children, and in **laryngitis** or **tracheitis**, syrup of ipecac is of great value. The following may be ordered for a child 3 years of age, 1-dram (4 c.c.) doses being given every one and one-half to three hours:—

℞ *Ammonii chloridi* gr. xlv (3 Gm.).
Tinctura opii camphorata . gr. lxxv (5 Gm.).
Syrupi ipecacuanha ℥c (7 Gm.).
Syrupi tolutani. f℥vj (25 Gm.).
Aqua anisi,
q. s. ad f℥iij (90 c.c.).

M.

To stimulate hepatic action the author gives the powdered extract of ipecac in capsules or pill form, never using the wine or tincture. S. Floersheim (Med. Standard, Dec., 1913).

In the treatment of **hemorrhage** it may be used alone or in combination with ergot or other antihemorrhagic agent. It is recommended that for this purpose ipecac be given in frequently repeated doses until vomiting ensues. It has been successfully used in **hemoptysis**, **epistaxis**, **menorrhagia**, etc. Subcutaneous injections of $\frac{2}{3}$ grain (0.04 Gm.) of emetine hydrochloride have been strongly recommended by Flandin, Joltrain, and others in hemoptysis. By the use of this alkaloid nausea and vomiting are avoided.

The wine of ipecac given in doses of 10 to 15 minims (0.6 to 1 c.c.) has been successfully used in **uterine in-**

ertia in the first and second stages of labor. For general use, however, other agents are superior.

Five cases of severe **hematemesis** and **melena**—in patients with **hepatic cirrhosis**, **ulcerative enterocolitis**, and **uremic ulcer of the stomach**—treated with subcutaneous injection of 1 grain (0.06 Gm.) of emetine hydrochloride after ordinary remedies had failed. Hemorrhage ceased and did not recur. By way of caution, injections of $\frac{1}{2}$ grain (0.02 Gm.) were given on the succeeding days. Another author found emetine ineffective in 2 cases of severe internal hemorrhage in typhoid fever, but observed cessation of an obstinate and abundant intestinal hemorrhage in a severe case of **jaundice** after 3 injections of $\frac{3}{4}$ grain (0.04 Gm.) of emetine hydrochloride, as well as in a case of recurrent **epistaxis**. L. Rénon, Lesné, and F. Ramond (Bull. et mém. de la Soc. méd. des Hôp. de Paris, Jan. 29, 1914).

Ipecac is used by the writer in diseases of the heart. In disorders of the auricle, which he believes are very often of toxic origin, ipecacuanha seems to be a valuable adjunct to digitalis. He prescribes $\frac{1}{2}$ grain (0.03 Gm.) of powdered digitalis, and $\frac{1}{8}$ grain (0.008 Gm.) of powdered ipecacuanha. Nausea is not hastened, and the effect of the digitalis seems to be improved. In a person with an untreated **fibrillation**, the pulse being very rapid and irregular, the writer orders powdered digipuratum, 18 grains (1.2 Gm.), and powdered ipecac, 5 grains (0.3 Gm.) made into 12 powders. One every 4 hours until 4 are taken; one every 6 hours until 4 are taken; and one every 8 hours until 4 are taken. Ipecacuanha has certain analogies to digitalis which suggest it as an adjuvant. L. F. Bishop (Med. Record, Aug. 31, 1918).

In **amebic dysentery** ipecac is so efficient as to be generally considered a specific. The most efficient mode of administering it appears to be to

give the alkaloid emetine in the form of the hydrochloride (*v.* **EMETINE**). Where the whole drug is used, it is best given in the dose of 40 grains (2.6 Gm.) in pills coated with phenyl salicylate and keratin, these coatings having for their purpose to prevent liberation of the drug until it reaches the intestine, nausea and emesis being thereby avoided. Where given without such a protective covering, the drug — often administered to the amount of 60 to 90 grains (4 to 6 Gm.) in severe cases—is expected to produce vomiting, after which small doses of 2 to 3 grains (0.13 to 0.2 Gm.) are given every hour, and continued until a profuse black stool occurs. This latter is a favorable prognostic sign, while its non-appearance is significant of danger. The great depression resulting from this mode of administration has to be counteracted by the free exhibition of stimulants. According to Wigglesworth, the preliminary use of $\frac{1}{2}$ -fluidounce (15 c.c.) doses of a saturated solution of magnesium sulphate and of 15-minim (1 c. c.) doses of dilute sulphuric acid every two hours, with a milk diet, completely prevents the nausea usually induced by ipecac. (See also **EMETINE**, Vol. IV.)

It is important to realize that emetine is a most powerful drug, having a toxic and cumulative action; therefore, the dosage and length of administration demand most careful consideration. In **amebic dysentery** 1 grain (0.06 Gm.) subcutaneously every day for 12 days will cure most cases, though some give $\frac{1}{2}$ grain (0.03 Gm.) daily by mouth as well, in keratin or salol-coated pills, making a total course of 18 grains (1.2 Gm.). Larger doses than this are not advised, and if amebic cysts are found afterward, the course should be repeated, but if possible not

within a month. The patients should be kept in bed, dieted, carefully watched and allowed up gradually. R. N. Chopra and B. N. Ghosh (Indian Med. Gaz., July, 1922).

In **amebic dysentery**, when, after a first course of emetine injections, diarrheal symptoms have disappeared, the writers give as a test 1 or 2 Segond's pills (each containing powdered ipecac, 0.066 Gm.; calomel, 0.033 Gm., and extract of opium, 0.008 Gm.). The patient then either has a slight exacerbation of his diarrhea, which disappears after a few more injections of emetine, or feels much better, in spite of which the treatment should be continued with smaller doses of emetine at longer intervals. Chronic enterocolitis or hepatic congestion occurring as complications are usually alleviated, temporarily at least, by emetine, which also has a definite preventive action against hepatic abscess. Ralli and Panayotatou (Presse méd., Aug. 29, 1923).

Emetine injections, although temporarily successful, do not eradicate an amebic infection from the bowel, even when given in almost toxic doses. Hence emetine bismuth-iodide and its modification, emetine periodide, have been largely employed and have proved themselves efficacious to a considerable extent in the acute, as well as in the chronic, stage with the passage of *E. histolytica* cysts. P. H. Manson-Bahr and R. M. Morris (Lancet, Sept. 12, 1925).

Ipecac has been found very useful in the treatment of that form of **acute hepatitis** which in the tropics eventuates in hepatic abscess and is due to the ameba of dysentery.

In the **diarrhea of cholera Asiatica** and **cholera morbus** ipecac, in the dose of 3 grains (0.2 Gm.), given every two hours, has been followed by good results.

The diaphoretic properties of ipecac are not infrequently utilized in the beginning of fevers, colds, and other

inflammatory conditions, for which purpose it is associated with opium, as in the official *pulvis ipecacuanhæ et opii*.

In **poison-ivy dermatitis** the free application of a wash consisting of 3 drams (12 Gm.) of powdered ipecac to a pint (500 c.c.) of water has been recommended by W. S. Gilmore. Neall recommends the use of 1 part of powdered ipecac in 8 parts each of alcohol and ether to relieve the inflammation caused by **mosquito bites**. Powdered ipecac made into a paste and smeared on the skin is said to relieve the pain and swelling produced by the **sting of bees**.

C. E. DE M. SAJOUS

AND

L. T. DE M. SAJOUS,
Philadelphia.

IRIS, CILIARY BODY, AND CHOROID, DISORDERS OF,—

The iris, ciliary body, and choroid, constituting the "uveal tract,"—the vascular or nutritive coat of the eye,—are best considered together.

The inflammations and degenerations that commonly affect the uveal tract are especially dependent on constitutional conditions which are often obscure, but which must be carefully hunted out and treated. The proper regimen or general treatment is often more important than local measures.

ANOMALIES OF THE IRIS AND CHOROID.—**Albinism.**—Absence of pigment in the uveal tract accompanies the lack of pigment in the hair and skin throughout the body. The iris has a dull, gray-blue color; the pupil by ordinary illumination may appear red. With the ophthalmoscope, red fundus-reflex may be seen through the iris, and the choroidal vessels are distinctly visible

against the yellowish-white background of the sclera. Such eyes usually present high errors of refraction, for which correcting lenses should be worn.

Aniridia is complete absence of the iris. By ordinary inspection it may seem uncertain what the condition of the interior of the eye really is. But with the ophthalmoscope the red of the fundus-reflex is obtained through every part of the cornea, interrupted by a smooth dark circle near the periphery of the reflex, the margin of the crystalline lens. It occurs either as a congenital anomaly, or after trauma causing extrusion of the iris or its folding back on the ciliary process.

Coloboma of the iris is an extension of the pupil usually downward. Generally the edge of the crystalline lens can be seen in the coloboma, and often it is slightly notched. The defect may extend back into the choroid, causing a white patch which may reach to the optic nerve. Such defects are often hereditary. Displacement of the pupil is called *corectopia*.

Coloboma of the choroid is a congenital lack of choroid in some part of the fundus. Sometimes it is merely a rounded area through which the sclera is seen; sometimes it extends from the equator of the eye back to or including the optic disk. It is to be distinguished from patches of choroidal atrophy or retinal exudation by its smooth, rounded margin. Partial coloboma may involve the superficial layers, leaving the larger vessels visible.

Persistent pupillary membrane, the remains of the fibrovascular membrane which closes the pupil during early fetal life, appears as one or more

threads that stretch across the pupil, or from the iris to an opaque area of the lens-capsule within the pupil. They are distinguished from posterior synechiæ by the fact that they arise not from the margin of the pupil, but from the front of the iris at some little distance from the pupillary margin.

Polycoria, multiple pupils, may be caused by division of the normal pupil into two by a band of persistent pupillary membrane, or it may be from openings in other parts of the iris. Only the central or true pupil is furnished with a sphincter muscle. Polycoria sometimes arises by atrophy of some parts of the iris, following injury and the formation of firm synechiæ in childhood.

IRITIS; CYCLITIS; IRIDOCYCLITIS.

Plastic inflammation of the iris and ciliary body includes iritis, cyclitis, iridocyclitis, parenchymatous and serous iritis, and the varieties of iritis named syphilitic, rheumatic, etc., according to the supposed cause.

Symptoms.—Pain in and about the eye, becoming severe, worse at night, and preventing sleep, is rarely absent. In poorly nourished women approaching middle life, what is called *quiet iritis* or *uveitis* occurs without pain and with little redness, so that the iris is firmly bound down to the lens capsule before the disease is noticed. Redness is seen in the pericorneal zone, and the color of the iris is altered and the pupil contracted by hyperemia. The iris is thickened and its surface dull. Vision is impaired by haziness of the media. Plastic exudate causes the iris to adhere to the anterior capsule of the lens, *posterior synechia*. When the ciliary body is

much involved, dots of exudate are deposited on the posterior surface of the cornea, usually on a triangular area at the lower part, *keratitis punctata*, and the ciliary region is tender to touch.

The synechiæ prevent the dilatation of the pupil under a mydriatic, the pupil therefore becoming irregular in shape. In a few cases the exudate into the iris and the formation of synechiæ occur while the pupil is partly dilated, and the usual contraction of the pupil is prevented.

ETIOLOGY.—Iritis may be caused by traumatism, but usually arises from some dyscrasia. Half of all cases are due to syphilis; other causes in the order of their frequency are rheumatism, anemia, acute febrile diseases, diabetes, gonorrhea, gout, and new growths in the iris. Autointoxication of gastrointestinal origin is an important cause of relapsing inflammations of the uveal tract. In syphilitic iritis occurs in the secondary stage within a year after infection. With rheumatism it may occur with or between other manifestations of the disease. It arises during convalescence from acute fevers. Patients who have latent gonorrhea are liable to attacks for many years after infection.

Recent observations seem to show that uveal inflammations are due to direct bacterial invasion of the uveal tract.

DIAGNOSIS.—Iritis and cyclitis quite often coexist. Iritis may be considered absent if there is no visible alteration of the iris and the pupil dilates widely and evenly under a mydriatic. Cyclitis is absent if there are no deposits on the cornea, or haziness of the vitreous, or tenderness of the ciliary region. Iritis and cyclitis

must be distinguished from keratitis by absence of change in the cornea; from glaucoma by the contracted pupil, and the absence of dilated scleral veins, increased tension or cupping of the optic disk; from panophthalmitis by the absence of swelling of the lids and dense opacity of the vitreous; from neuralgia by the redness of the eye and the alteration of the iris; from conjunctivitis by the slight swelling and freedom from discharge of the conjunctiva. The alterations in the pupil are best seen with the ophthalmoscope or after the use of a mydriatic. In general the pupil is distorted and irregular in shape. But these irregularities may be slight and difficult to make out when the pupil is small and adherent to the lens capsule all round its margin.

PROGNOSIS AND SEQUELÆ.

—Iritis is a slow, painful disease, dangerous to the future usefulness of the eye. Eyes that do well may take many weeks to recover, and pain may continue or increase many days after efficient treatment is begun. It is liable to relapse or recur, especially in rheumatic or cachectic patients. When the whole margin of the pupil is bound down to the lens, *exclusion of the pupil*, the forward current of fluid from the posterior chamber is obstructed, pushes forward the iris, and causes secondary glaucoma. Extensive plastic deposits about the lens and in the vitreous are followed by softening and shrinking of the eyeball with detachment of the retina, blindness, and degenerative changes in all parts of the eye. Few cases of iritis recover absolutely, although many eyes remain quiet and useful throughout life. The greatest danger

is from recurring attacks, if the general condition causing the uveal inflammation be not recognized and overcome.

Sometimes iritis causes a myopia that may last for some months.

TREATMENT.—The eye should be promptly put under the influence of a mydriatic, preferably **atropine**, which should be continued until the eye is free from redness, except in a few cases of cyclitis without iritis, which do better with the pupil undilated. The prevention and breaking up of synechiæ by such a drug is usually of greatest importance. The eyes should be given complete rest, and protected from sudden changes of light. **Dark glasses** may be worn in the sunlight. The general nutrition of the patient is so important that confinement to a dark room should not be continued more than a few days. Pain may be relieved by **bathing the eye with very hot water** from three to five minutes several times a day; or by taking blood from the temple. Sometimes **dionin** gives much relief. It should be used once or twice a day, either in powder or a 5 per cent. solution.

The treatment of the general or constitutional condition underlying the attack of iritis is of equal or greater importance than the local treatment, and is much more frequently neglected.

Internally **calomel** should be given, irrespective of the cause of the iritis, until the bowels have freely moved, and **mercury** continued by **inunction** or in other forms in the syphilitic cases. Whatever constitutional condition is present is to be carefully treated, and tonics used to build up the general condition.

The influence of **salvarsan** is strik-

ingly favorable, sometimes producing in a few days a cure that would have required as many weeks or even months under older methods. It should, however, be followed by a prolonged course of **mercury**. In iritis arising from autointoxication **calomel** may be continued, in doses sufficient to keep the bowels loose, for several weeks, care being taken to avoid other manifestations of mercurial poisoning. **Diet** should be carefully regulated. **Hot** or **Turkish baths** repeated at intervals of one, two, or more days, according to the acuteness of the symptoms and the strength of the patient, are very useful. Large doses of **sodium salicylate** may be given for a few days in acute cases. **Pilocarpine** sweats may be useful in more chronic conditions.

Iridectomy.—The excision of a part of the iris may be required for the sequels of iritis, as exclusion of the pupil or extensive synechia; for *occlusion* of the pupil, its closure by a deposit of lymph; for corneal opacity in front of the pupil, some part of the cornea remaining clear; for partial opacity of the lens; or for glaucoma.

Location.—If done to secure a clear passage for light through the dioptric media—*optical iridectomy*—it must be located so light can enter through the best dioptric surfaces, must be as small as will remain subsequently unobstructed, and must be exposed when the lids are opened. If it is merely to free the iris from its adhesions, or open up a passage from the posterior to the anterior chamber, or for glaucoma, it should be placed where it will ordinarily be hidden as much as possible beneath the lids. For glaucoma it should be large, including one-fifth of the circumference of the iris,

and should extend up to the ciliary margin.

Technique.—An incision is made in the cornea between the location for the iridectomy and the corneal margin, slightly longer than the width of the iridectomy and parallel to the corneal margin. This is made either with a narrow Graefe knife or a lance-shaped keratome. A pair of iris-forceps is introduced and the iris seized near its pupillary margin, and the part so caught is drawn outside the corneal incision. Sometimes the iris can be better separated from adhesions by a blunt iris-hook which is pressed upon the pupillary edge of the iris until it catches under it, and draws it out through the corneal incision. A sufficient portion of the iris having been drawn out, it is cut off with fine scissors, the stump is returned within the eye, care being taken to free it entirely from the corneal incision; and the eye is closed with a light dressing until the corneal wound ceases to allow the escape of the aqueous. Usually but a few hours are required for this.

Iridectomy should not be done for the sequelæ of iritis until long after the eye has become free from redness or irritability.

CHOROIDITIS.

Plastic inflammation and atrophy of the choroid is more of a chronic degenerative process than an acute inflammation. It often accompanies similar inflammation of the iris and ciliary body, and is variously designated *choroiditis*, *iridochoroiditis*, and *choroidal atrophy*.

VARIETIES.—When one or two large areas of the choroid are affected at once it is called *diffuse choroiditis*. When small areas are affected, the

remainder of the choroid being normal, it is called *localized choroiditis* if only one or two patches appear, or *disseminated choroiditis* if there are several. When the region of the macula is involved it is called *central choroiditis*, and a form of the central occurring in old persons is called *senile*. The process may affect only the superficial layer of the choroid, or it may involve the deeper layer.

SYMPTOMS.—Only the appearances revealed by the ophthalmoscope are characteristic of this disease, although it may be attended with discomfort or aching in and about the eyes, flashes of light, impairment of vision by scotomata, or clouds due to vitreous opacities. In the early stages of exudation the choroid may be swelled; it is lighter and yellower than normal, and may be veiled by haziness of the vitreous, but there are no pigment deposits. Later, as the process passes on to atrophy, the margins and parts included in the affected area show brown or black pigment deposits, between which may be seen the large vessels of the deep layer of the choroid or the white sclera. Throughout the disease the retinal vessels run over the affected area undisturbed. When the atrophy and pigment deposits are complete, the appearances produced tend to continue throughout life.

ETIOLOGY.—The causes of inflammation of the iris and ciliary body similarly affect the choroid. Especially is it liable to present lesions due to syphilis or tuberculosis. In addition, it is liable to suffer from eye-strain in hyperopia, astigmatism, and most extensively in myopia. Excessive use of the eyes and exposure to excessive light and heat, especially

when habitually concentrated on one part of the choroid, are also important causes.

DIAGNOSIS.—Choroiditis is recognized with the ophthalmoscope by the color and pigmentation of the affected areas. It has to be distinguished from exudation or opaque nerve-fibers in the retina which hide all detail of the pigment layer and some parts of the retinal vessels, and from coloboma of the choroid, which has a smooth margin where parts of the largest choroidal vessels may be seen against a white background.

PROGNOSIS.—Choroidal inflammation is always serious. Its obscure, persistent causes, difficult of recognition and removal, make it generally a disease likely to continue until it has done very grave damage to the eye. It is worth every effort to permanently check its progress. Cases where it is localized and does not involve the macula are the most favorable, and may end in cure without noticeable impairment of vision.

TREATMENT.—Complete rest for the eyes, often under a mydriatic, is important, with protection from sudden changes or great excess of light, or exposure to heat. This will sometimes require a change of occupation, as the giving up of cooking or blacksmithing. **Correcting lenses** must be constantly worn, and during the acute stage much use of near vision should be avoided. The underlying dyscrasia must also receive efficient treatment, for upon this will depend the persistence and extension of the disease and the ultimate results. Syphilis should be combated by the prolonged use of **mercury**; with, sometimes, **iodides** late in the disease. A **general tonic regimen** is generally

required. **Outdoor life** is beneficial, and on account of its depressing influence upon general nutrition, prolonged confinement to a dark room should be carefully avoided.

UVEAL TUBERCULOSIS is of more frequent occurrence than was formerly supposed. It is usually secondary to a tuberculous focus situated elsewhere in the body. When chronic, its prognosis is comparatively good under efficient treatment for the general disease, especially under the use of **tuberculin**.

The **iris** is commonly involved in children. Small, isolated, gray nodules appear scattered throughout that membrane; these are attended with the ordinary symptoms of iritis. If the cause be not recognized and effectively treated, the iris becomes bound down by posterior synechiæ, and vision reduced to light perception by lesions of the deeper parts of the eye, before the disease becomes quiescent.

Tuberculosis of the choroid may be either acute or chronic. The **acute** condition arises in acute general tuberculosis of children and young persons, during the last few days or weeks of life. The choroidal involvement is quite common, but is only revealed by the ophthalmoscopic examination and will escape notice unless carefully looked for. The tubercles are seen as oval or rounded yellowish spots, devoid of pigmentation, and one-half the size of the optic disk or less.

Chronic tuberculosis of the choroid may take either of two distinct forms. A large mass or tumor may develop, presenting most of the symptoms of other choroidal tumors. This form is rare, but its nature has long

been recognized. In the other form the tubercles are small, occur singly or one or two at a time successively, run their course in a few weeks or months, and leave a patch of choroidal atrophy with marked pigment deposits. Such lesions occur in young or even older adults. They are not very rare, but only recently has it been recognized that they are of tuberculous origin.

DIAGNOSIS.—The appearance of the lesions, though suggestive, is not characteristic. The iris nodules are seen in children, while those of syphilis appear later in life. The patches of choroidal tubercle have quite indefinite borders, and are at first free from pigment. Later the pigment appears in the midst of the patch rather than about its margin.

But the diagnosis must rest chiefly on the various tests with tuberculin. These are of great value. Only after skin tests and tuberculin injections have repeatedly failed to give local or general reactions, can this cause be excluded. The focal reaction may be noticeable on close examination of the uveal lesion in a minority of cases. It is the most convincing proof of the nature of the process.

PROGNOSIS.—This has been completely changed by the recognition of the nature of these lesions and the development of tuberculin therapy. Without such treatment the eye was greatly damaged or lost. With it the great majority of eyes improve and continue useful; and in some cases recovery is practically complete.

TREATMENT.—This includes the general regimen for tuberculosis, with special care not to use the eyes for close work, and **atropine** for acute inflammatory manifestations. A series

of **tuberculin** injections should be given, beginning with very small doses given about once a week, and continued over many months, or one or more years. Until the general liability to tuberculous lesions is overcome the eye will not be safe from recurrences.

PURULENT INFLAMMATION OF THE IRIS, CILIARY BODY, AND CHOROID.—Although in grave plastic iritis hypopyon may appear, the exudate becoming largely purulent, these cases running the general course of plastic iritis require no separate consideration. A totally distinct clinical picture is presented when general suppuration of the uveal tract occurs. The condition is then called *suppurative choroiditis*, or *iridochoroiditis*, or from its involvement of all parts of the eye, *panophthalmitis*.

SYMPTOMS.—The disease begins with great disturbance of vision, pain in and about the eye, and general redness. The conjunctiva, the lids, and often the tissues of the orbit become greatly swelled. Haziness of the vitreous quickly prevents any view of the fundus, and the eye rapidly becomes entirely blind. The pain continues to increase until the sclero-corneal coat is perforated, allowing exit to the contained pus. Then pain rapidly diminishes, the swelling goes down, and the eyeball soon shrinks to a small, sightless, and generally harmless stump: *phthisis bulbi*.

ETIOLOGY.—Suppuration of the uveal tract arises from infected wounds, either accidental or operative; from perforating ulcer or abscess of the cornea; or thrombosis of the orbital veins in orbital cellulitis. It may also be produced by metastasis or em-

bolism in connection with abscess in other parts of the body; in pyemic conditions, puerperal sepsis, or erysipelas, or in cerebrospinal meningitis, influenza, scarlatina, and other acute specific fevers.

DIAGNOSIS.—The disease cannot escape notice unless masked by previous inflammation of the orbit, erysipelas of the lids, or suppuration of the cornea; or unless it occur in the course of exhausting disease, when the local reaction may be slight, and the loss of vision unnoticed by the dull or unconscious patient. It is to be distinguished from other ocular inflammations by the opacity of the vitreous and rapid loss of sight, or when it supervenes upon corneal ulcer, by increase of pain and swelling.

PROGNOSIS.—Most cases run a rapid course to complete blindness and phthisis bulbi. In a few the reaction is less severe and a purulent accumulation in the vitreous simulating in appearance glioma of the retina remains indefinitely. Such cases are called *pseudoglioma*. In a very few cases in children, where the purulent chorioiditis follows specific fevers, and especially cerebrospinal meningitis, some sight is retained, and the vitreous humor may subsequently clear up to a considerable extent.

TREATMENT.—Pain is most promptly relieved and the disease cut short by **enucleation of the eye**; but this has in a few cases been followed by death from meningitis. Some authors believe that the risk of meningitis is increased by enucleation; but this is very doubtful if proper care is taken to cleanse the wound and secure free drainage.

When, because of the patient's condition or disinclination, enucleation

cannot be done, the eye should be **poulticed**, and after two or three days opened by a free **incision across the cornea** that will permit the escape of the crystalline lens and all purulent accumulations. Analgesics, such as **morphine** and **acetanilid**, may be necessary until the eye is opened. If the eye retains some sight, poulticing is improper; **rest**, **atropine**, and **bleeding** from the temple are indicated. Even where the eye is blind, but the pain and swelling not severe, as in *pseudoglioma*, it may be wise to defer operation until the general health is improved.

TUMORS OF THE UVEAL TRACT.—This is a not very unusual seat of secondary tumors, although they may attract little attention, appearing late and growing slowly. The following are the principal primary new growths:—

Cyst of the iris is apt to follow a penetrating wound in which a bit of epithelium or eyelash has been implanted on the iris. It may have the form of a serous cyst occupying a large part of the anterior chamber, or an epithelial pearl on the surface of the iris. Either form may cause secondary glaucoma. It should be **excised**.

Gumma may develop in the iris, causing one or more rounded swellings, attended with iritis; or in the ciliary body, where it is also attended with inflammation, and may cause ciliary staphyloma either from its primary swelling or by thinning of the overlying sclera by absorption so that it cannot resist intraocular pressure. In the iris it usually leaves a thinned and atrophied spot through which may in some cases be seen the fundus-reflex. Active antisyphilitic

treatment is indicated. **Salvarsan** causes rapid improvement.

Ossification of the choroid is often found in eyeballs that have long been blind, and have undergone extensive degenerative changes. It may cause sympathetic irritation, but not inflammation, of the fellow-eye.

Sarcoma may arise primarily in either part of the uveal tract. In the iris it appears as a tumor which grows very slowly, usually brown and deeply pigmented, sometimes of lighter color, with visible vessels.

Sarcoma of the ciliary body may first manifest itself in the pupil or by pushing forward the iris; or it becomes adherent to the iris and by its growth drags the iris away from its ciliary attachment, revealing the tumor beneath.

Sarcoma of the choroid starts as a rounded displacement of the retina, which is not wavy like an ordinary detachment, and through which large vessels may be seen.

For many months or years uveal sarcoma grows slowly, giving rise to no other symptoms; this is its first, or latent, stage. Then it causes increased tension of the eyeball and inflammation: the second, or inflammatory, stage. The third stage begins when it perforates the sclera and begins to invade neighboring tissues. It now grows rapidly. The fourth stage begins with the extension of the disease by metastasis to other organs.

Diagnosis.—In the early stage the ophthalmoscopic examination revealing the tumor, and its repetition at sufficient intervals showing increase in the size, gives definite and reliable information. After the retina becomes detached it is very difficult to determine if the detachment be pri-

mary or due to the tumor. In this stage transillumination of the eyeball through the sclera may be of great importance. When the retinal detachment is accompanied with increased tension of the eyeball the presence of a tumor is very probable. Exploratory or partial operations are to be avoided, owing to the danger of favoring extension or metastasis.

Treatment.—The earliest possible removal of the tumor is indicated. In a few cases of sarcoma of the iris this may be accomplished by **iridectomy**, removing the growth with the iris from which it springs. In all other cases the eye must be **enucleated**, and if perforation of the sclera has occurred the orbit should be emptied of its contents.

Carcinoma of the choroid is always secondary and occurs at an advanced stage of the primary disease. Nevertheless in a few cases the examination of an eyeball enucleated for tumor has occasionally led to the diagnosis of cancer, and the first recognition of the presence of the primary growth in some other organ. If the carcinomatous nature of the tumor is known, its **removal** is only justified to give relief from pain, since lesions elsewhere will prove fatal before the tumor in the eye causes other complications.

EDWARD JACKSON,
Denver.

IRON.—Iron (*ferrum*) is a metallic element occurring widely in nature, both in the animal and vegetable kingdoms and in inorganic compounds, chiefly iron oxide, carbonate, sulphide, and silicate. From its ores iron is extracted by first roasting in air, then reducing the resulting oxide with carbon.

As described in the U. S. Pharmacopœia, iron occurs in the form of fine, bright, non-elastic wire. The preparation of pure iron universally used, however, is "reduced iron," made by heating ferric oxide, Fe_2O_3 , in a stream of hydrogen gas, the latter taking up the oxygen of the oxide to form water and leaving a fine, blackish, odorless, and tasteless powder, insoluble in water and alcohol, but dissolving in mineral acids with the formation of salts.

Iron compounds are also known as chalybeates, or martial preparations (Mars: god of war). Mineral springs containing iron supply the so-called chalybeate waters. Two series of iron compounds exist—the ferrous, usually greenish in color, and containing a relatively large proportion of the metal, and the ferric, generally of a reddish-brown or, in dilute solutions, yellow color.

PREPARATIONS AND DOSES.

—The official iron preparations may be conveniently classified in three groups: First, the bland, or those devoid of energetic local effects, which may be subdivided into three classes, the insoluble and soluble solids and the liquids; second, the astringent or styptic; and third, the compound, in which there enters another active medicinal agent in addition to the iron:—

I. Bland Preparations.

(a) Solids Insoluble in Water.

Ferrum reductum (reductum, B. P.; reduced iron), required to contain not less than 90 per cent. of pure iron. Dose, 1 grain (0.06 Gm.).

Ferri carbonas saccharatus (saccharated ferrous carbonate), containing not less than 15 per cent. of ferrous carbonate [FeCO_3]. It is made by dissolving 5 parts of ferrous sulphate in hot distilled water, $3\frac{1}{2}$ parts of sodium bicarbonate in warm distilled water,

filtering the two solutions, adding the former to the latter, washing the resulting precipitate repeatedly with hot distilled water, mixing it intimately with 8 parts of sugar, evaporating to dryness on a water bath, reducing it to a powder, and mixing with it, if necessary, enough dried sugar to make 10 parts. The product is a greenish-brown powder, odorless, sweetish and then ferruginous in taste, only in part soluble in water, but dissolving completely upon the addition of hydrochloric acid, forming a yellowish liquid. Dose, 4 grains (0.25 Gm.).

Pilula ferri carbonatis (pills of ferrous carbonate; Bland's pills), made by rubbing up 8 parts of potassium carbonate with a little glycerin and water, adding 16 parts of granulated ferrous sulphate and 4 parts of sugar, previously triturated, and rubbing the mass thoroughly into it, assumes a greenish color. One part each of tragacanth and althea are then incorporated and, if necessary, a little more water added, to produce a mass of pilular consistence. If these pills are to be kept they must be coated, as they undergo change after a short time, becoming oxidized and turning red. Dose, 2 to 5 pills.

Massa ferri carbonatis (mass of ferrous carbonate; Vallet's mass), made by dissolving 100 parts of ferrous sulphate and 46 parts of monohydrated sodium carbonate separately in boiling distilled water, adding syrup to the iron solution, filtering and cooling both, gradually introducing the iron solution into the carbonate solution, washing the resulting precipitate with syrup and distilled water, expressing the water from it, mixing it with 38 parts of clarified honey and 25 parts of sugar, and evaporating the product on a water bath,

with constant stirring, until it is reduced to 100 parts by weight. Dose, 4 grains (0.25 Gm.).

Ferri hypophosphis, N. F. (ferric hypophosphite), $[\text{Fe}(\text{H}_2\text{PO}_2)_3]$, a grayish powder, odorless and almost tasteless, practically insoluble in water, more readily soluble in the presence of dilute hypophosphorous acid or in a warm, concentrated solution of the citrate of an alkali metal,—with which it forms a green solution,—and freely soluble in hydrochloric acid. Dose, 3 grains (0.2 Gm.).

(b) *Solids Soluble in Water.*

Ferri phosphas solubilis (soluble ferric phosphate; iron phosphate with sodium citrate), $[\text{Fe}_2(\text{PO}_4)_2 + \text{Na}_3\text{C}_6\text{H}_5\text{O}_7]$, containing at least 12 per cent. of metallic iron, and occurring in bright-green scales, with an acidulous, slightly saline taste, freely soluble in water, and insoluble in alcohol. It becomes discolored upon exposure to light. Dose, 4 grains (0.25 Gm.).

Ferri et ammonii citras (iron and ammonium citrate), $[(\text{NH}_4)_3\text{Fe}(\text{C}_6\text{H}_5\text{O}_7)_2]$, containing not less than 16 per cent. of iron, and occurring in garnet-red scales having a saline, slightly ferruginous taste, deliquescent in moist air, and freely soluble in water. Dose, 4 grains (0.25 Gm.).

Ferri glycerophosphas, N. F. (ferric glycerophosphate), containing a variable quantity of $\text{Fe}_2(\text{C}_3\text{H}_7\text{O}_6\text{P})_3$ corresponding to from 14 to 16 per cent. of iron, and occurring as yellowish-green, transparent scales or a greenish-yellow powder, odorless and nearly tasteless. It dissolves slowly in about 2 parts of water, and is insoluble in alcohol. Dose, 3 grains (0.2 Gm.).

Ferri pyrophosphas solubilis, N. F. (soluble ferric pyrophosphate; iron pyrophosphate with sodium citrate),

$[\text{Fe}_4(\text{P}_2\text{O}_7)_3 + \text{Na}_3\text{C}_6\text{H}_5\text{O}_7]$, containing not less than 10 per cent. of metallic iron, and occurring in apple-green scales, with an acidulous, slightly saline taste, and freely soluble in water. Dose, 4 grains (0.25 Gm.).

Ferri lactas, N. F. (ferrous lactate; iron lactate), containing not less than 97 per cent. of $\text{Fe}(\text{C}_3\text{H}_5\text{O}_3)_2 \cdot 3\text{H}_2\text{O}$, and occurring as a greenish-white crystalline powder, or in crystalline masses, with a slight, characteristic odor and a mild, sweet and ferruginous taste. It dissolves slowly but almost completely in 40 parts of water at 25° C., in 12 parts of boiling water, and is freely soluble in solutions of alkali citrates, yielding a green solution; almost insoluble in alcohol. Dose, 5 grains (0.3 Gm.).

Ferrum albuminatum, N. F. (albuminized iron; iron albuminate), a compound of iron oxide and albumin, rendered soluble by the presence of sodium citrate, and containing 17 to 19 per cent. of iron. It occurs in reddish brown, lustrous granules or a brown powder, is almost or quite odorless, is freely soluble in water, yielding dark solutions, and is almost insoluble in alcohol. Dose, 8 grains (0.5 Gm.).

Ferrum peptonatum, N. F., (peptonized iron; iron peptonate), a compound of iron oxide and peptone, rendered soluble by the presence of sodium citrate, and containing 16 to 18 per cent. of iron. It occurs in dark brown, lustrous granules or a brown powder, has a slight characteristic odor, is freely soluble in water, yielding dark solutions, and is almost insoluble in alcohol. Dose, 5 grains (0.3 Gm.).

Ferri citras, U. S. P. VIII (ferric citrate), $[\text{Fe}_2(\text{C}_6\text{H}_5\text{O}_7)_2 + 6\text{H}_2\text{O}]$, pure enough to contain at least 16 per cent.

of metallic iron, and occurring in thin, reddish-brown scales, slightly ferruginous in taste, slowly but completely soluble in cold water, and insoluble in alcohol. Dose, 4 grains (0.25 Gm.).

Ferri et ammonii tartras, U. S. P. VIII (iron and ammonium tartrate), $[(\text{NH}_4)_3\text{Fe}(\text{C}_4\text{H}_4\text{O}_6)_3]$, not less than 13 per cent. of iron, and occurring in garnet-red to reddish-brown scales, having a sweetish, slightly ferruginous taste, and very soluble in water. Dose, 4 grains (0.25 Gm.).

Ferri et potassii tartras, U. S. P. VIII (iron and potassium tartrate; tartrated iron), $[\text{Fe}_2\text{O}_3 \cdot \text{K}_2(\text{C}_4\text{H}_4\text{O}_6)_2]$, not less than 15 per cent. of iron, and occurring in garnet-red to reddish-brown scales, having a sweetish, ferruginous taste, and freely soluble in water. Dose, 4 grains (0.25 Gm.).

(c) *Fluid Preparations.*

Liquor ferri et ammonii acetatis (solution of iron and ammonium acetate; Basham's mixture), made by adding to 50 parts of the official solution of ammonium acetate, 6 parts of dilute acetic acid, 4 parts of tincture of ferric chloride, 12 parts each of aromatic elixir and of glycerin, and finally enough water to make 100 parts. Dose, 4 fluidrams (16 c.c.).

Mistura ferri composita, N. F. IV (compound iron mixture; Griffith's mixture), made by rubbing up 18 parts each of myrrh and sugar and 8 parts of potassium carbonate with 700 parts of rose water, adding 60 parts by volume of spirit of lavender and 6 parts of ferrous sulphate, the latter previously dissolved in rose water, and finally adding enough rose water to make 1000 parts by volume and mixing thoroughly. Dose, 4 fluidrams (16 c.c.).

Vinum ferri, N. F. IV (wine of iron), made by dissolving 4 parts by weight of iron and ammonium citrate in 70 parts by volume of white wine, adding 6 parts of tincture of sweet orange-peel and 10 parts of syrup, and finally adding enough white wine to make 100 parts; the mixture is to be set aside two days, then filtered. Dose, 2 fluidrams (8 c.c.).

II. Astringent Preparations.

(a) *Solids.*

Ferri chloridum (ferric chloride; iron perchloride, sesquichloride, trichloride), $[\text{FeCl}_3 + 6\text{H}_2\text{O}]$, containing not less than 20 per cent. of metallic iron in the form of chloride, and occurring in orange-yellow, crystalline pieces, with a strongly astringent taste and perhaps a faint odor of hydrochloric acid. It deliquesces in moist air, is freely soluble in water and in alcohol, and melts to a reddish-brown liquid at 96° F. (35.5° C.). Dose, 1 grain (0.06 Gm.).

Ferri sulphas (ferrous sulphate; copperas), $[\text{FeSO}_4 + 7\text{H}_2\text{O}]$, occurring as large bluish-green crystals with a saline, astringent taste, freely soluble in water, but insoluble in alcohol. The crystals effloresce in dry air, become coated through oxidation with a brownish layer of basic ferric sulphate when exposed to moist air, and lose 6 molecules of the water of crystallization when heated to 239° F. (115° C.). Dose, 1½ grains (0.1 Gm.).

Ferri sulphas exsiccatus (exsiccated or dried ferrous sulphate), $[\text{approximately } 2\text{FeSO}_4 + 3\text{H}_2\text{O}]$, made by heating the preceding on a water-bath, constantly stirring, until the product is reduced to between 64 and 65 per cent. of its initial weight, and powdering the residue. The latter is grayish white and dissolves slowly but completely in water. Dose, 1 grain (0.06 Gm.).

Ferri sulphas granulatus (granulated ferrous sulphate; precipitated ferrous sulphate) [$\text{FeSO}_4 + 7\text{H}_2\text{O}$], made by dissolving ferrous sulphate in boiling distilled water, adding dilute sulphuric acid and filtering while hot, concentrating the solution by evaporation, and precipitating it by the addition of alcohol. The product is a pale, bluish-green, crystalline powder, soluble in alcohol. Dose, $1\frac{1}{2}$ grains (0.1 Gm.).

Ferri et ammonii sulphas, U. S. P. VIII (ferric ammonium sulphate; ammonioferric alum), [$\text{FeNH}_4(\text{SO}_4)_2 + 12\text{H}_2\text{O}$], not less than 11.5 per cent. of metallic iron, and occurring in violet, efflorescent crystals with an acid and astringent taste, soluble in 3 parts of water, but insoluble in alcohol. Dose, $7\frac{1}{2}$ grains (0.5 Gm.).

(b) *Liquids.*

Liquor ferri chloridi (solution of ferric chloride), containing not less than 10 per cent. nor more than 11 per cent. of iron, and made by heating iron wire with hydrochloric acid, filtering, adding more hydrochloric acid, mixing with nitric acid, warming again, removing the nitric acid, and adding hydrochloric acid and water to make a specified volume of solution. The product is a yellowish-brown liquid, with an acid, strongly astringent taste and acid reaction. Dose, $1\frac{1}{2}$ minims (0.1 c.c.).

Liquor ferri tersulphatis (solution of ferric sulphate or iron tersulphate or sesquisulphate), [$\text{Fe}_2(\text{SO}_4)_3$], corresponding to 10 per cent. of iron. It is made in much the same manner as the next preparation, but with different ratios of the ingredients. Used in the preparation of ferric hydroxide, and of ferric hydroxide with magnesium oxide (arsenic antidote).

Liquor ferri subsulphatis, N. F. (solution of ferric subsulphate, iron persul-

phate or basic iron sulphate [approximately $\text{Fe}_4\text{O}(\text{SO}_4)_5$]; Monsel's solution), a preparation of variable chemical composition, containing an amount of the basic sulphate corresponding to not less than 20 nor more than 22 per cent. of metallic iron. It is made by treating ferrous sulphate with hot sulphuric and nitric acids, destroying the nitric acid, and diluting to the proper concentration, and occurs as a reddish-brown liquid, strongly styptic and acid, miscible with water and alcohol in all ratios without decomposition. Dose, 3 minims (0.2 c.c.); used chiefly locally.

III. Compound Preparations.

(a) *Solids.*

Ferri et quininae citras, U. S. P. IX (soluble iron and quinine citrate), containing 11.5 per cent. of quinine and 13.5 per cent. of iron, and occurring in greenish, golden-yellow, bitter and deliquescent scales, rapidly soluble in cold water, and partly soluble in alcohol. Dose, 4 grains (0.25 Gm.).

Ferri et strychninae citras, U. S. P. VIII (iron and strychnine citrate), not less than 0.9 nor more than 1 per cent. of strychnine and 16 per cent. of iron, and occurring in garnet-red to yellowish-brown scales, with a bitter, mildly ferruginous taste, deliquescent when exposed to moist air, soluble in water and partly soluble in alcohol. Dose, 2 grains (0.125 Gm.).

Pilulae aloes et ferri, N. F. (pills of aloe and iron), made by mixing 7 Gm. (108 grains) each of aloe, dried ferrous sulphate and aromatic powder, incorporating enough confection of rose to make a mass, and dividing into 100 pills. Dose, 2 pills.

Pilulae ferri iodidi, N. F. (pills of ferrous iodide [FeI_2]), each containing enough of the iodide to yield $\frac{1}{3}$ grain

(0.04 Gm.) of metallic iron and $\frac{5}{16}$ grain (0.05 Gm.) of iodine, together with licorice, balsam of Tolu, sugar, etc. Dose, 2 pills.

(b) *Liquids.*

Ferri hydroxidum cum magnesi oxido (ferric hydroxide with magnesium oxide; arsenic antidote), made by mixing 10 fluidrams (40 c.c.) of the official solution of ferric sulphate (liquor ferri tersulphatis) with 4 fluidounces (125 c.c.) of water, rubbing 150 grains (10 Gm.) of magnesium oxide with cold water to a smooth mixture, transferring the latter to a 1-quart (liter) bottle, filling it three-fourths full with water, and shaking. Just before use, the magnesia mixture is added gradually to the iron solution in another bottle, and the whole shaken. Dose, 4 fluidounces (120 c.c.).

Syrupus ferri iodidi (syrup of ferrous iodide), containing about 5 per cent. of ferrous iodide, and occurring as a pale-green liquid with a sweet, strongly ferruginous taste and a slightly acid reaction. Dose, 15 minims (1 c.c.).

Elixir ferri, quinina et strychnina phosphatum, U. S. P. VIII (iron, quinine and strychnine phosphates), each fluidram (4 c.c.) of which contains about 1 grain (0.06 Gm.) of ferric phosphate, $\frac{1}{2}$ grain (0.03 Gm.) of quinine and $\frac{1}{60}$ grain (0.001 Gm.) of strychnine. Dose, 1 fluidram (4 c.c.).

Glyceritum ferri, quinina et strychnina phosphatum, U. S. P. VIII (glycerite phosphates of iron, quinine and strychnine), each 15 minims (1 c.c.) of which contains about $1\frac{1}{4}$ grains (0.08 Gm.) of soluble ferric phosphate, 2 grains (0.12 Gm.) of quinine phosphate, and $\frac{1}{80}$ grain (0.0009 Gm.) of strychnine. Dose, 15 minims (1 c.c.).

Syrupus ferri, quinina et strychnina phosphatum, N. F. (syrup of phos-

phates of iron, quinine and strychnine), containing per fluidram (4 c.c.) about $1\frac{1}{4}$ grains (0.08 Gm.) of soluble ferric phosphate; $1\frac{1}{10}$ grains (0.12 Gm.) of quinine phosphate, and $\frac{1}{80}$ grain (0.0009 Gm.) of strychnine phosphate. Dose, 1 fluidram (4 c.c.).

Vinum ferri amarum, N. F. IV (bitter wine of iron), made by dissolving 5 parts of soluble iron and quinine citrate in 50 parts of white wine, adding 6 parts of tincture of sweet orange-peel and 30 parts of syrup, and finally adding enough white wine to make 100 parts. Dose, 2 fluidrams (8 c.c.).

Among the other preparations containing iron which are or have been recognized in the National Formulary, the following may be mentioned:—

Elixir ferri pyrophosphatis, quinina et strychnina (N. F.). Dose, 1 fluidram (4 c.c.).

Elixir ferri, quinina et strychnina (N. F.). Dose, 1 fluidram (4 c.c.).

Elixir gentiana et ferri (N. F.). Dose, 1 fluidram (4 c.c.).

Elixir gentiana et ferri phosphatis (N. F.). Dose, 1 fluidram (4 c.c.).

Elixir malti et ferri (N. F. IV). Dose, 4 fluidrams (16 c.c.).

Extractum ferri pomatum (N. F.), (ferrated extract of apples; crude malate of iron). Dose, 10 grains (0.6 Gm.).

Liquor ferri albuminati (N. F.). Dose, 2 fluidrams (8 c.c.).

Liquor ferri citratis (N. F.). Dose, 10 minims (0.6 c.c.).

Liquor ferri peptonati (N. F.). Dose, 2 fluidrams (8 c.c.).

Liquor ferri peptonati et mangani (N. F.). Dose, 2 fluidrams (8 c.c.).

Liquor ferri salicylatis (N. F.), (solution of ferric salicylate), containing 12.5 per cent. each of sodium salicylate

and tincture of ferric citrochloride. Dose, 2 fluidrams (8 c.c.).

Liquor zinci et ferri compositus (N. F. IV). Used locally and externally as antiseptic, astringent and deodorant.

Syrupus calcii lactophosphatis et ferri (N. F.). Dose, 1 fluidram (4 c.c.).

Syrupus ferri saccharati solubilis (N. F.). Dose, 1 fluidram (4 c.c.).

Syrupus ferri lactophosphatis (N. F. IV). Dose, 1 fluidram (4 c.c.).

Syrupus ferri et mangani iodidi (N. F. IV). Dose, 15 minims (1 c.c.).

Syrupus ferri citro-iodidi (N. F. III), (tasteless syrup of iodide of iron). Dose, 30 minims (2 c.c.).

Tinctura ferri chloridi atherea (N. F.), (Bestuscheff's tincture; Lamotte's tincture). Dose, 30 minims (2 c.c.).

Tinctura ferri citrochloridi (N. F.), (tasteless tincture of iron, not reacting with tannin). Dose, 8 minims (0.5 c.c.).

Tinctura ferri pomata (N. F.), (tincture of ferrated extract of apple). Dose, 1 fluidram (4 c.c.).

Vinum pruni virginianae ferratum (N. F. IV). Dose, 1 fluidram (4 c.c.).

Following are some of the unofficial iron preparations more or less commonly in use:—

Ferropyrin (ferripyrin) $[(C_{11}H_{12}N_2O)_3.(FeCl_3)_2]$, a compound consisting of approximately 36 per cent. of ferric chloride and 64 per cent. of antipyrin, and occurring as a yellowish-red powder, with an acid and astringent taste, soluble in 5 parts of water and in alcohol. Dose, 5 grains (0.3 Gm.). As an injection it may be used in a 1 or 1.5 per cent. solution, and as a hemostatic in a 20 per cent. solution or in dry form.

Ferric salicylate, occurring as a violet-gray powder, slightly soluble in

water. Dose, 3 to 10 grains (0.2 to 0.6 Gm.).

Ferric manganese citrate (iron and manganese citrate), occurring in brown scales, very slightly soluble in hot water. Dose, 3 to 10 grains (0.2 to 0.6 Gm.).

Soluble ferric arsenite (ferric arsenite and ammonium citrate), containing 1.4 per cent. of arsenic and about 15 to 18 per cent. of iron, and occurring in freely soluble green scales. It is suitable for subcutaneous injection. Dose, $\frac{1}{2}$ to 1 grain (0.03 to 0.06 Gm.).

Triferrin (ferric paranucleinate), a compound prepared by treating cows' milk casein with pepsin and precipitating the solution with a ferric salt. It contains 22 per cent. of iron, 9 per cent. of nitrogen, and 2.5 per cent. of phosphorus in organic combination, and occurs as a tasteless powder, soluble only in dilute alkalies. Dose, 5 grains (0.3 Gm.).

Arsentriferrin, an arsenoparanucleate of iron standardized to contain 0.1 per cent. of arsenic, together with about 16 per cent. of iron and 2.5 per cent. of phosphorus in organic combination. It occurs as an orange-colored, tasteless powder, soluble only in dilute alkalies. Dose, 5 grains (0.3 Gm.).

Ferratin (sodium ferrialbuminate), prepared from egg albumin and pure iron salts, and containing 6 per cent. of iron in organic combination. It occurs as a light-brown, tasteless powder, soluble in dilute alkalies. Dose, $7\frac{1}{2}$ grains (0.5 Gm.).

Arsenoferratin (sodium arsenoferrialbuminate), similar to the preceding, but with arsenic introduced into the ferrialbuminic acid to the extent of 0.06 per cent. It occurs as a brown, tasteless powder, soluble in water. Dose, $7\frac{1}{2}$ grains (0.5 Gm.).

Ovoferrin, a 5 per cent. solution of an artificial proteid product—formed by electrolysis of serum albumin—with “masked” iron present to the extent of 0.4 per cent. The solution is reddish brown in color, slightly aromatic in taste, contains 9 per cent. of alcohol, and is incompatible with alkalies, though not with acids. Dose, 2 to 4 fluidrams (8 to 16 c.c.).

Hemogallol, an organic iron compound produced by precipitating dilute defibrinated blood with a saturated solution of pyrogallol, and occurring as a reddish-brown, insoluble, and nearly tasteless powder. Dose, 4 to 8 grains (0.25 to 0.5 Gm.).

Hemol (parahemoglobin; reduced hemoglobin), an organic iron compound produced through the reduction of blood by shaking it with zinc dust and water, and said to contain iron to the extent of about 3 per cent. It occurs as a dark-brown, insoluble, nearly tasteless powder. Dose, 2 to 8 grains (0.12 to 0.5 Gm.).

Hemoglobin (red coloring matter of the blood), occurring as a brownish-red powder or in scales, soluble in water. Dose, 75 to 150 grains (5 to 10 Gm.) daily in wine or syrup.

MODES OF ADMINISTRATION.—Oral.—In the anemias iron should be used in a non-astringent form, viz., as reduced iron or the official pill of ferrous carbonate (Blaud’s pill). Insoluble preparations such as these are considered the most efficient therapeutically. Where it is desired to prescribe iron in solution, the soluble phosphate, the double citrate of iron and ammonium, and the double tartrate of iron and potassium are most useful. The “scale salts” of iron, i.e., the salts of the vegetable acids, such as the two last mentioned, are for the most part

neutral in reaction, and can be prescribed either in neutral, alkaline or acid solutions; the scale salts containing alkaloids such as quinine and strychnine, however, cannot be prescribed in alkaline solutions, without precipitation of the alkaloids (Foreman and Gertler). The salts of the mineral acids, e.g., the chloride and sulphates, are acid in reaction and should be prescribed in acid solutions. The least constipating preparations of iron are iron lactate and the double tartrate of iron and potassium (Henry).

Iron need not be given oftener than three times a day, as its absorption is slow at best. Small doses of iron, such as $\frac{1}{4}$ to $\frac{1}{2}$ grain (0.015 to 0.03 Gm.), are often quite as effective as the larger amounts generally prescribed, and less apt to upset the stomach (Hare).

The official tincture of ferric chloride is a most disagreeable compound to take. A better form is the simple dilution of the official liquor ferri perchloridi to the strength of the tincture and the addition of glycerin. A formula which the author has used for a long time is:—

<i>R. Liq ferri perchloridi</i>35 parts,	}
<i>Aque destil-</i>		
<i>late</i>65 parts,	
		q. s. ad f3x (40 c.c.).
<i>Glycerini</i> f3ij	(8 c.c.).

The strength of this is slightly less than that of the tincture. When given with milk—10 to 30 drops in 10 to 30 drams of milk—this makes a palatable mixture, which does not attack the teeth and undoubtedly, from the strong affinity of the perchloride for proteids, contains some “masked” or changed iron differing from the perchloride. In **anemia** in general this mixture will give good results, and for that following or attending **rheumatism** it is the remedy *par excellence*. R. E. Van Gieson (N. Y. Med. Jour., April 11, 1908).

The syrup of the iodide of iron is acid in reaction, diluted hypophosphorous acid being used in its preparation. It can, however, be prescribed with Fowler's solution, as neither the acid nor alkali are enough in excess to cause precipitation; the alkali of the one neutralizes the acid of the other, forming a comparatively neutral solution. In the pill of the iodide of iron reduced iron and iodine combine to form ferrous iodide. These pills should always be freshly prepared, as the iron readily oxidizes, becoming ferric iodide, which is very difficult of assimilation. W. H. Foreman and J. H. Gertler (Jour. Ind. State Med. Assoc., Oct., 1909).

In **chlorosis** and chlorotic forms of **secondary anemia** the following recommendations as to treatment, in addition to rest and diet, are made by the author:—

When gastric irritation is not present, the following mixture may be given:—

℞ *Ferri sulphatis*. gr. iij (0.2 Gm.).
Magnesium sulphatis 3j (4 Gm.).
Acidi sulphurici diluti ℥v (0.3 c.c.).
Syrupi aurantii. 3j (4 c.c.).
Aquæ chloroformi .q. s. ad 3j (30 c.c.).

M. Sig.: Three times a day after meals.

Or,

℞ *Liquoris ferri perchloridi* .. ℥xv (0.9 c.c.).
Magnesium sulphatis 3j (4 Gm.).
Glycerini 3j (4 c.c.).
Aquæ chloroformi .q. s. ad 3j (30 c.c.).

M. Sig.: Three times a day after meals.

If there is slight irritability of the stomach, instead of the above acid preparations, one of the following may be given:—

℞ *Pilula ferri carbonatis* gr. v (0.3 Gm.).
Extracti aloes . gr. ss (0.03 Gm.).

Ft. in pil. no. j.

Sig.: Two to be taken three times a day after food.

Or,

℞ *Ferri sulphatis exsiccati* gr. ij (0.13 Gm.).
Extracti aloes . gr. ss (0.032 Gm.).
Extracti rhamni purshiana ... gr. j (0.065 Gm.).

Ft. in pil. no. j.

Sig.: Three times a day after meals.

When irritability of the stomach is marked, it is advisable to give at first one of the scale preparations of iron, e.g.:—

℞ *Ferri et ammonii citratis*. gr. viij (0.52 Gm.).
Sodii bicarbonatis gr. x (0.65 Gm.).
Syrupi aromatici 3j (4 c.c.).
Aquæ chloroformi .q. s. ad 3j (30 c.c.).

M. Sig.: Three times a day after meals.

A laxative pill to be taken at night.
W. H. Willcox (Practitioner, Sept., 1913).

When the stomach rebels against inorganic iron, ferratin may be advantageously given with milk or other liquid food. It is quite suitable for children, to whom one-half the adult dose of it may readily be given. Otoferrin is another useful preparation, which is not dissociated by the gastric juice into the astringent chloride of iron and therefore fails to affect the digestion, though asserted to have in noticeable degree the property of exciting the appetite. Arsenoferratoze, hemogallol and hemol are among the numerous other available preparations.

Hypodermic.—The citrate of iron is as good as, if not superior to, any other preparation for hypodermic use. The

dose generally employed is 16 minims (1 c.c.) of a 10 per cent. solution. If injected into the buttocks or muscles of the back this generally causes a sharp pain, which lasts for some time. According to Lépine this inconvenience may be avoided by using a larger quantity (40 minims—2.5 c.c.) of a weaker (4 per cent.) solution, only slight tenderness resulting. Other compounds of iron that have been used hypodermically are the citrate of iron and ammonium, the citrate of iron and manganese (15 minims or 1 c.c. of a 20 per cent. solution—Da Costa), peptonized iron (25 minims or 1.6 c.c. of a 10 per cent. solution on alternate days—Rosenthal), and iron cacodylate ($\frac{1}{2}$ to $\frac{3}{4}$ grain or 0.03 to 0.045 Gm. daily—Gilbert and Lereboullet). Ferric citrate, sodium cacodylate (containing arsenic), and strychnine sulphate are frequently injected in combination.

Intravenous.—Intravenous injections of iron have been recommended by Aporti and others for the purpose of causing a rapid and marked increase of hemoglobin percentage. The soluble double salts should alone be used, in order to prevent precipitation of the blood albumins, and the injection should be given carefully and slowly, to avoid central nervous depression. The indications for this route of introduction would appear to be quite limited. According to Grocco, the intravenous are no more efficacious than hypodermic injections.

Rectal.—Defibrinated bullock's blood has been given by enema in cases of gastric intolerance to iron. The hypodermic route is, however, to be preferred.

INCOMPATIBILITIES.—Iron is incompatible with all astringent vegetable preparations, which contain tannin

and form with iron the tannate, an intensely black compound. Calumba and quassia are the only commonly bitter tonics that may be combined with iron. Ferrous salts form green precipitates with alkalies and alkaline carbonates, lime water, magnesia, and the carbonates of calcium and magnesium. They are also incompatible with salts of mercury, silver, and gold, sulphides, chromates, and oxidizing agents such as potassium permanganate and hydrogen dioxide. Ferric salts form brown precipitates with the alkalies, alkaline earths and their carbonates, and are also incompatible with albumin, readily oxidized alkaloids such as morphine and apomorphine, sulphides, sulphates, thio-sulphates, and hypophosphites; iodides and hydriodic acid; guaiacol, salicylates, and resorcinol; guaiac, aloin, and the essential oils of cloves, cinnamon, gaultheria, and thyme. Ferric salts turn mucilage of gum arabic into a gelatinous material.

CONTRAINDICATIONS.—Internal use of iron is contraindicated in pronounced organic disease or marked irritability of the gastrointestinal mucous membrane (Knott). Autointoxication and constipation are serious impediments to the favorable action of iron compounds (Van Gieson), and should be overcome in so far as is possible before and during the use of this drug. Iron is said to be contraindicated when pulmonary hemorrhage exists or threatens, as well as in all acute pulmonary affections.

According to Elsner, mere symptoms of dyspepsia do not contraindicate iron, but in such cases functional investigation of the stomach should precede the use of the drug. Iron is contraindicated in organic stomach diseases with hyperacidity or hyper-

secretion, and likewise if existing dyspeptic troubles are increased by its use.

Knott has warned that iron should not be used in convalescence from typhoid fever or dysentery till a considerable period has elapsed, and then only with caution; nor should it be prescribed in the anemia which frequently accompanies intestinal irritability in tuberculosis.

The use of iron may be dangerous in anemias associated with gastric symptoms, in which an examination of the stools for occult blood to exclude the presence of ulceration should always be made before prescribing it, and in anemias of tuberculous origin, in which it may activate the morbid process by increasing oxidation. Certain cases of chlorosis in association with tuberculosis are benefited, but in the average case of pulmonary tuberculosis it only serves to aggravate the condition. H. Huchard and C. Fiessinger (*Revue de thérap. médico-chir.*, March 15, 1910).

Lépine advises caution in the administration of citrate of iron hypodermically where the kidneys are not sound, since even where they are healthy injections that are too concentrated may lead not only to the usual harmless polyuria, but to anuria and even nephritis. Such treatment is altogether contraindicated in anemic patients suffering from hepatic cirrhosis, epistaxis, hemorrhoids, metrorrhagia, etc., as it predisposes to hemorrhages.

PHYSIOLOGICAL ACTION.

—**Locally**, iron in the form of simple inorganic salts such as ferric chloride, acts as an astringent by reacting with the protein of the tissues—including the blood—to form a precipitate of iron albuminate. The latter soon constitutes a protective layer over the deeper tis-

ues, keeping them from being corroded by the dissociated acid portion of the salt, *e.g.*, the chloride ion. The albuminate of iron, the various forms of "organic" or undissociable iron, and the double salts of iron fail to precipitate tissue proteins, and therefore differ fundamentally in their local action from the simple iron salts, being both non-astringent and devoid of irritating properties.

The iron salts of the mineral acids are more astringent, more permanent, more easily affected by tannin and other iron precipitants, precipitate albumins more readily, are perhaps more readily absorbed, and have a more irritant effect upon the digestive organs than the salts of the vegetable acids. Foreman and Gertler (*Jour. Ind. State Med. Assoc.*, Oct., 1909).

General Effects.—Information as to the direct effects of iron upon the nervous system, circulation, etc., can be obtained only by injecting intravenously one of its non-astringent double salts, such as the double tartrate of iron and sodium, for upon administration by other routes absorption is too slow to yield acute effects and if a *simple* inorganic salt were given intravenously the blood would be clotted through precipitation of its proteins, thrombosis resulting. Experimentation in animals has shown that the direct action of iron upon the nervous system is manifested in primary irritation, followed by paralysis, of the latter. The heart and vessels are but little affected by iron, which can therefore not be said to exert an astringent effect by causing vasoconstriction. The gastrointestinal tract, however, is apparently specifically irritated by iron, the mucous membranes of this canal proving, in the experimental animals, to be the seat of marked

swelling and congestion, at times even accompanied by localized hemorrhages. Vomiting frequently occurs, and the appearance of blood in the vomitus and feces is sometimes noted. The kidneys also seem to be subject to a special unfavorable influence on the part of iron, repeated injection of small amounts of iron citrate having been found by Kobert to cause renal congestion, albuminuria and the elimination of casts. The respiration is at first accelerated by iron given intravenously, then becomes slow and difficult. Death in acute experimental iron poisoning occurs from asphyxia the result of central respiratory paralysis.

Taken by mouth, iron fails to produce any evident general effects in the normal organism, even when ingested in inorganic form and in large amount. The symptoms noted after excessive doses are those of direct gastrointestinal irritation, due to the astringency of the compounds introduced. Even upon continued use of only moderate doses, the same action is exerted, imperfect digestion, constipation and abdominal pain being the results. Iron preparations tend to augment the acid secretion of the stomach (Buzdygan).

Absorption of ingested iron, whether in inorganic or organic form, takes place chiefly from the duodenum. It is believed that in the stomach iron, in whatever form taken, is for most part changed to the chloride (ferrous chloride—Cervello) owing to the presence of hydrochloric acid in this organ. Next it combines with protein material to form albuminates; then, entering the duodenum, is either taken up in solid form by leucocytes and the intestinal epithelial cells or absorbed in solution. The old theory that only "organic" compounds of iron—*i.e.*, those containing it

in a "masked" state so that its presence is not revealed by ordinary test reagents such as ammonium sulphide and potassium dichromate—could be absorbed from the alimentary tract, has been conclusively disproved by Kunkel, Gaule, and others. The amount permanently absorbed, however, is never very large, most of the iron ingested passing directly out with the stools and an additional considerable proportion being later re-excreted into the bowel after absorption. Animal experimentation has revealed that whereas, after the administration of iron by mouth, the duodenal epithelium as well as that of the upper part of the jejunum shows granules of iron deposited in its constituent cells, that of the stomach, the lower part of the jejunum, and the ileum does not contain such granules. The metal soon after passes into the mesenteric lymph-glands and the spleen, but several days later is found to have again migrated, being now present in largest amount in the liver and in the epithelium of the colon, including the cecum. That iron absorbed actually does become deposited for a time in the liver has been directly proven by comparing the content of iron in the livers of young animals fed on milk alone with that in the livers of others fed on milk to which iron had been added; the amount of iron was found greater in the latter series of animals than in the former. Where there is a deficiency of hemoglobin some of this iron, which may originally have been administered in inorganic form, is very probably built up in the liver to hemoglobin, an intermediate stage in this conversion being the organic iron compound known as ferratin.

In addition to its storage in the spleen and liver, iron has been observed to become deposited in the bone-marrow

upon intravenous injection of its compounds in animals. Some have attributed to it a specific power to stimulate the blood-forming organs, exemplified in the rapid improvement witnessed in cases of chlorotic anemia to which inorganic iron has been given. That the increased activity of these structures, however, is not merely the result of addition of raw material necessary for the carrying out of their hematopoietic function has not been conclusively proved.

According to P. H. C. Fowell, in all persons there is an excess of iron in the blood over that which is combined with hemoglobin; normally, such excess bears a ratio, to the total amount of iron, averaging 4.2 to 1. In pernicious anemia the ratio is markedly altered, approaching 2 to 1.

In pernicious anemia, as observed by Chalie, Nové-Josserand, and Boulud, there is a constant and marked siderosis or deposit of iron in the spleen and liver. In pulmonary tuberculosis siderosis is constant in the spleen, but very slight or absent in the liver, even though the latter is cirrhotic. In non-tuberculous cirrhosis there is siderosis in both spleen and liver.

Absorbed iron is excreted by the cecum and colon, only a negligible amount passing out through the kidneys. Since the body does not normally require more than about 10 mgm. daily, it is hard to see why 200 times this amount is beneficial in certain anemias. In their clinical tests with reduced iron the writers used an electromagnet to separate the metallic iron and oxides of iron—which had passed through the bowel unabsorbed—from the non-magnetic iron compounds absorbed and then re-excreted by the gut. Among a group of patients whose hemoglobin percentage remained unchanged or even declined upon exhibition of iron, 68 to 83 per cent. of the iron was found by this method to appear in the feces unchanged, while among another group, in which the hemoglobin rose under iron treatment, the discharge of unchanged iron in the feces

was as much as 18 per cent. lower. Folkmar and Ulrich (*Ugeskr. f. Læger*, Dec. 27, 1923).

Examining the organs of infants for iron, the writers found that at birth there begins a deposition of iron in the liver and spleen, ascribable to birth injuries and the consecutive hemorrhages. The maximum deposits are reached between the 1st and 2d months, whereupon a decline occurs, until after the 5th month no iron is histologically demonstrable. Schwartz, Baer and Weiser (*Zeit. f. Kind.*, Feb. 19, 1924).

Infants fed on an exclusive milk diet after the 8th or 9th month may develop a rather severe anemia, presumably due to lack of iron and also, possibly, of pigment in the food. It is very desirable to add iron at an early age to the diets of infants suspected of having an insufficient iron deposit. For this purpose iron-containing food is considered more efficient than inorganic iron, possibly because the former also contains pigment, which is as necessary for hemoglobin formation as is iron. Of all vegetables, spinach is the only one efficient in small amounts as a source of iron. Egg yolk is important. Of the fruit sauces, prune sauce contains a surprisingly large amount of iron. It is not easy to make up a practical dietary for an infant of 1 year which will contain the required 2 mgm. of iron without these foods. L. W. Hill (*Boston Med. and Surg. Jour.*, Aug. 21, 1924).

Experiments in rats and dogs showing that inorganic iron, given by mouth, subcutaneously or intravenously, is absorbed and may be found especially in the liver and spleen, but is not converted into hemoglobin. Animals made anemic by one or several large bleedings do not recover any more rapidly when iron is given. On the other hand, the efficiency of food iron is very pronounced. C. S. Williamson and H. N. Ets (*Arch. of Int. Med.*, Sept., 1925).

The commercial "peptonized" iron (a mixture of ferric oxide and peptone) and other similar preparations have

been asserted to stimulate the leucocytes to invade the epithelial layer of the intestinal villi. This fact may have some relation to the absorption of the drug.

Excretion of absorbed iron, as already intimated, is a relatively slow process, and takes place almost exclusively through the epithelium of the large intestine. No increase over the very small amount normally excreted through the kidneys is observable after administration of additional iron medicinally. Neither does it pass out from the liver into the intestinal tract with the bile, whence it is inferred that whatever iron is to be excreted is conveyed to the intestinal epithelium through the blood-stream. According to Hochhaus and Quinke, excretion of iron previously accumulated in the submucous tissue of the large intestine is probably effected through the extrusion of iron-laden leucocytes.

The amount of iron normally absorbed from the food, as well as the quantity excreted daily, have both been shown to be very small. While the total weight of iron in the body of an adult is about 40 to 55 grains, the amount absorbed from the food each day is only about $\frac{1}{12}$ to $\frac{1}{6}$ grain. Stockman found $\frac{1}{8}$ grain in the diet of a young lady living in the ordinary way and taking an average amount of food, while in that of 2 chlorotic girls who ate very little the quantity averaged $\frac{1}{25}$ grain a day. The total excreted daily by all channels is correspondingly small—less than $\frac{1}{10}$ grain, of which only $\frac{1}{20}$ to $\frac{1}{40}$ grain passes out in the urine.

In experiments performed by Skvortzoff to ascertain the effect of medicinal administration of iron on nitrogenous metabolism in the healthy organism, no pronounced action in this direction was

observed. Daily doses of 5 to $7\frac{1}{2}$ grains caused a very slight decrease in the assimilation of the nitrogenous portions of the food.

UNTOWARD EFFECTS AND POISONING.—Unfavorable results from the use of iron are practically limited to gastrointestinal irritation, the production of a sensation of fullness and abnormal warmth in the head, or frontal headache, and occasionally, epistaxis or hemorrhage from the throat or lungs, particularly in the presence of lung tuberculosis. Constipation, indigestion, and gastric pain are the most frequent of the gastrointestinal disturbances produced. Tachycardia, precordial discomfort, insomnia, and an acneiform or erythematous itching eruption are other conditions that have been attributed to the administration of iron. Bladder irritation causing frequent micturition and, in children, enuresis are at times caused by it.

Serious acute poisoning from iron is not likely to occur unless it be from intravenous injection, absorption by other routes being too slow to permit of dangerous general toxic effects. Lépine reports, however, that a little over 45 grains (3 Gm.) of the citrate injected hypodermically, has produced vomiting, fever, and malaise lasting several hours. Kobert has described a pathological condition which he terms the "metallic kidney," the result of an attempt of the kidneys to eliminate an excess of iron in the blood, and which consists of an accumulation of the metal in the epithelial cells of the convoluted tubules; this may be so marked as to produce evident obstruction in the tubular lumen.

Case of a woman hospitalized for typhoid fever. Being recently from Japan, the only food she would take was rice gruel, upon which she gradually became exceedingly emaciated

and anemic. Iron citrate, $\frac{3}{4}$ grain (0.05 Gm.), was ordered hypodermically. The first dose, on the 48th day of the disease, was followed by a chill, rise of temperature to 102° F., with pulse corresponding. After 2 days' interval without iron, the same dose was followed by a chill, temperature of 105°, and rapid defervescence. No more iron was given, and the temperature remained at 99° or below to recovery. The remaining ampules of iron citrate in the same box were used on another patient without causing any reactions. F. F. Gundrum (Cal. State Jour. of Med., Oct., 1922).

Pronounced and even lethal gastroenteritis may result from ingestion of excessive amounts of the more irritating iron salts such as Monsel's salt and ferric chloride.

Morgenstern, in a detailed study of the effects of various iron preparations on the teeth, found that ferratin, iron albuminate, reduced iron, and a solution of the saccharate of iron and manganese had no deleterious action whatever, that ferric citrate and the waters of some chalybeate springs exerted a very mild caustic effect and that tincture of ferric chloride, ferrous sulphate, ferrous lactate, and the waters of certain other iron-bearing springs caused a more or less marked decalcification of the teeth and imparted to them a brown color. The chloride and iodide of iron were found particularly prone to awaken toothache, producing this effect in a few days, where predisposition already exists, even in a 1:1000 solution.

Prophylaxis and Treatment.—The most important prophylactic measure is to overcome constipation both before and during the administration of iron by the use of laxative remedies. The latter, *e.g.*, aloes, are sometimes given in the same preparation with the iron,

but as this tends to accelerate unduly the passage of the iron itself out of the intestinal tract, it is preferable to administer the laxative separately.

In the event of intense irritation of the mucous membranes by iron salts, baking soda, soap, or tannic acid are useful as antidotes.

Injury to the teeth from iron may be avoided either by employing only the compounds known to be inoffensive in this particular, by ordering the solution to be taken through a glass tube, or, if a solid preparation is to be used, by prescribing it in gelatin-coated pills or capsules.

THERAPEUTICS.—The most important indication for the exhibition of iron is the presence of certain forms of **anemia**, viz., those in which the hemoglobin of the blood is present in less amount than normal. Moreover, this applies particularly in those varieties in which the hemoglobin index, or relation of hemoglobin percentage to percentage of red corpuscles, is low, *i.e.*, in **chlorosis** and chlorotic forms of anemia, such as are commonly met with in tuberculosis, syphilis, malignant disease and many other conditions. Anemias, the result of hemorrhage, chronic poisoning by lead, mercury, and arsenic, the presence of parasites in the intestine, or the pullulation of malarial organisms in the blood are also benefited by iron, though special attention must be paid in these conditions to removal of the original cause of the anemia.

Hemoglobin may be deficient either because of defective hematopoiesis (formation of blood) or by reason of excessive hemolysis (destruction or breaking up of the red corpuscles). The best results with iron are obtained in cases belonging to the former class. In **progressive pernicious anemia**,

however, iron has been thought sometimes to be productive of some good when given in combination with arsenic.

Most cases of chlorosis are completely cured by iron, the condition of the blood being not alone corrected, but subsidiary phenomena such as edema, gastric disorder, and amenorrhea caused to disappear indirectly owing to the restoration of the hemoglobin to an adequate level. According to A. Hofmann the iron acts by stimulating the process of blood-formation in the bone-marrow, although in normal animals (not those rendered anemic by blood-letting) he found only some increase in the number of red cells circulating, and of the fat in the bone-marrow, without any increase of cell formation in the marrow. Where hemoglobin is deficient, according to this investigator, iron accelerates the ripening and entrance into the circulation as non-nucleated cells of the young erythrocytes produced in the bone-marrow.

Treatment with iron ought to be continued, as a rule, from six weeks to two months, in order to procure all its useful effects. All three types of anemia—toxic, infectious, and hemorrhagic—should be treated that length of time. In **toxic anemia**, such as **chlorosis**, two essentials precede the prescription of iron—the restoration of the gastric functions by the use of diet and absorbent powders, and the regularization of the bowels. Laxatives should be ordered, to be combined later with iron. The following formulæ are useful:—

℞ *Iron and potassium tartrate* gr. iss (0.09 Gm.).
Pulverized rhubarb,
Heavy magnesia,
 of each gr. j (0.06 Gm.).
Extract of cinchona ... gr. iss (0.09 Gm.).

M. et ft. pil. no. j. Sig.: Two to be taken before meals.

℞ *Ferrous carbonate* gr. iss (0.09 Gm.).
Aloes gr. ½ (0.02 Gm.).
Extract of rhubarb gr. j (0.06 Gm.).
 M. et ft. pil. no. j. Sig.: Two to be taken before meals.

℞ *Iron and potassium tartrate,*
Extract of rhubarb,
Extract of gentian,
 of each gr. lxxv (5 Gm.).
Extract of nux vomica. gr. viij (0.5 Gm.).
 M. et ft. pil. no. vj. Sig.: Two to be taken at meals.

Metrorrhagia due to anemia in young girls can often be stopped by giving the following in pill form:—

℞ *Ferrous carbonate* gr. iss (0.09 Gm.).
Ergotin gr. j (0.06 Gm.).
Quinine hydrobromide . gr. ¼ (0.01 Gm.).
Extract of belladonna-leaves gr. ¼₁₂ (0.005 Gm.).
 M. et ft. pil. no. j. Sig.: Two to be taken before meals.

Huchard and Fiessinger (*La thérap. en vingt médicaments*; N. Y. Med. Jour., Feb. 28, 1911).

As for the dose of iron required in anemias, small amounts such as 1 or 2 grains (0.06 or 0.12 Gm.) of reduced iron or the carbonate three times daily are generally sufficient, any larger quantity being useless to the organism and merely tending to increase gastrointestinal irritation. Where the tongue is heavily coated, the breath offensive, and the bowels constipated, the administration of iron should be preceded by a purge (Henry). It is to be borne in mind, too, that where gastric hyperacidity already exists, iron may aggravate the dyspeptic symptoms, unless the digestive affection has been set right before it is ordered (Buzdygan). Where

hydrochloric acid secretion is, on the other hand, diminished, iron is often of service in improving the appetite and gastric functions. For these purposes ferrous sulphate is one of the best preparations to use, though in some cases the stomach may prove intolerant of it. Where feeble digestion and constipation coexist the addition of aloes to iron, as in the *Pilula aloes et ferri*, N. F., is recommended. A combination introduced by Squire under the appellation "Mistura ferri laxans" may also be ordered under these circumstances.

℞ *Ferri sulphatis* gr. ij (0.12 Gm.).
Magnesii sulphatis .. ʒj (4 Gm.).
Acidi sulphurici diluti. ʒiij (0.2 c.c.).
Spiritus chloroformi . ʒlxx (1.25 c.c.).
Aquæ menthæ pipē-
itæq.s. ad fʒj (30 c.c.).—M.

In cases of anemia in which a prompt and intense effect of iron is desired, or where iron is not tolerated by the gastrointestinal tract, hypodermic administration has been widely availed of. For further information concerning methods of prescribing iron the reader is referred to the section on MODES OF ADMINISTRATION.

Because of the undoubted efficacy of the lactate of iron the writer agrees with Lindberg's contention that organic iron preparations may produce results as good as do inorganic preparations, provided large doses are used. The usual organic preparations, however, are those in which the iron is bound in protein combinations that do not set free the iron ions. It is these free ions which enhance blood production. With the lactate, however, the iron does ionize, and this preparation thus behaves in this connection like the inorganic salts. C. Sonne (*Acta med. Scandin.*, May 31, 1922).

In **chlorosis** iron may be regarded as a specific, provided a daily dose corresponding to at least 0.1 Gm. (1½ grains) of metallic iron be given. Use-

ful preparations are reduced iron, 0.1 to 0.2 Gm. (1½ to 3 grains) daily, the *ferri oxidum saccharatum*, N. F., ½ dram (2 Gm.) 3 times daily, and a solution of ferratin. Bland's pills frequently pass out unchanged. The dosage should be increased for a week, maintained for about 6 weeks, then gradually reduced. Lenhartz has recommended the following soft pills:

℞ *Ferri sulphatis*. ʒiiss (10 Gm.).
Magnesii oxidi gr. xxvii (1.75 Gm.)
Glycerini gtt. lxxx.

Ft. pil. No. c.

The drug should always be taken after meals. P. Morawitz (*Minch. med. Woch.*, June 23, 1922).

The inorganic iron salts are especially powerful stimulants to the hematopoietic organs and counteract the depression of regeneration of the blood cells which exists in **chlorosis** probably on account of a deficiency of hormones originating in the ovaries. The *tinctura ferri pomati*, N. F., is recommended, in a dosage of 10 drops after each meal; likewise, the following pills:—

℞ *Ferri lactatis* . gr. xlv (3 Gm.).
Gentianæ pul-
veris gr. ix (0.6 Gm.).
Extracti gen-
tianæ gr. xxvii (1.8 Gm.).

Ft. pil. No. xxx.

Chalybeate mineral waters are frequently more active than other iron preparations, notwithstanding their very small iron content. F. Müller (*Deut. med. Woch.*, June 23, 1922).

The inorganic iron compounds may be absorbed, but if they are too much ionized local corrosion may occur. On the other hand, if the metal is bound too firmly, as in some of the much used organic preparations, it may go through the intestine unabsorbed. The writers regard Bland's pills and the salts of the organic oxyacids as serviceable. Fischler and Paul (*Zeit. f. klin. Med.*, Mar. 20, 1924).

In fresh mineral waters the author found with the X-ray some very labile iron compounds which he regards as

possibly constituting the form in which iron is operative in blood production. (Oppenheimer (Klin. Woch., Jan. 8, 1926).

Neuralgia due to anemia is greatly benefited by large doses of the tincture of ferric chloride (30 minims—2 c.c.) or of the saccharated carbonate (20 grains—1.3 Gm.), given three times daily. Ferripyridin, a red crystalline compound of iron with antipyrin, might also be used in doses of 4 to 8 grains (0.25 to 0.5 Gm.) in these cases. **Amenorrhea** dependent upon anemia is benefited by the citrate of iron, either alone or combined with strychnine. The **dysmenorrhea** often occurring in anemic young women is also overcome by iron (Parsons).

In the anemia of **malaria**, if the spleen is enlarged and the portal circulation engorged, a purge, *e.g.*, compound jalap powder, with or without podophyllin, should precede the administration of iron. According to Schussler, Prussian blue (ferric ferrocyanide) possesses antiperiodic as well as tonic properties, and may be substituted for quinine in doses of 5 grains (0.3 Gm.) every three hours where the former fails.

In **anemia due to lead**, iron is useful in association with the iodides.

In anemia accompanying **sypilis** the use of the iodide of iron is indicated. Henry has recommended the following:—

R *Tr. ferri chloridi* ... f3ss (15 c.c.).
Hydrargyri chloridi
corrosivi gr. j (0.06 Gm.).
Glycerini f3ss (15 c.c.).
Aqua f3iij (90 c.c.).

M. Sig.: One teaspoonful in water thrice daily after meals.

In 19 cases of **postinfluenzal anemia**, the condition was usually of the chlorotic type. Reduced iron was always

given, often in a powder containing 1 grain (0.06 Gm.) of iron and $\frac{1}{2}$ grain (0.03 Gm.) of sucrose. The usual dosage was 1 grain of iron 3 times daily. Effects on the mouth were avoided by giving the iron just before meals. In 70 per cent. of the cases the hemoglobin was doubled within 2 months; in 25 per cent. it was trebled, and in 2 patients was quadrupled in 6 weeks. The real improvement was not as rapid as the apparent gain. The action of inorganic or metallic iron in large doses is deemed by the writer quite different from that of organic compounds in small doses, the therapeutic effect being seemingly due rather to the large dosage than the form of iron administered. Reduced iron does not lead to intolerance, and is valuable likewise in the **anemia attending lactation** and in mild **cryptogenetic anemias**. G. Lindberg (Acta med. Scandin., lvi, 162, 1922).

Similarly in the various manifestations of scrofula, especially **tuberculous adenitis**, as well as in **rachitis**, the iodide of iron, given in syrup form, is frequently of considerable benefit. It is best to begin with small doses, the amount being then increased as tolerance is established. In rachitis, a combination of the phosphates of iron and calcium is preferred by some to the iodide. Addition of iron to codliver oil has been stated to increase the efficiency of the former in these cases.

According to Smith, in **chlorosis** it is often the emetic effect of iron sulphate that is of value. During **convalescence** or when the derangement has subsided after severe indigestion, the tongue being pale, indented, and silvery, the acid preparations of iron are especially indicated. **Rickets** and **splenic anemia** show improvement most quickly with acid preparations—ferrous chloride or sulphate. In **tuberculous bone or gland disease** in children, he obtained the best results from a mixture of the tincture of ferric chloride, 5 to 10 drops (0.3 to 0.6 c.c.), with the B. P. solution ($\frac{1}{2}$ grain to the ounce) of mercury perchloride, from 10 to

20 drops (0.6 to 1.2 c.c.), taken perseveringly three times a day for months.

In **pulmonary tuberculosis** iron is generally considered to be contraindicated where hemoptysis threatens. Combined administration of digitalis and iron has, however, been recommended to control the hectic fever in this affection, 5 drops of tincture of digitalis and 10 drops of tincture of ferric chloride being given three or four times daily.

In **heart disease** iron is undoubtedly of considerable value where anemia exists, whether the cardiac affection be of valvular or musculo-degenerative nature. Among valvular affections, **aortic and mitral insufficiencies** appear to benefit most from its use. Special care is necessary, however, to avoid inducing gastric disturbance and constipation with it—effects particularly likely to be noted where venous stasis already exists.

In **chronic nephritis** iron in the form of Basham's mixture (*Liquor ferri et ammonii acetatis*), 2 to 4 fluidrams (8 to 16 c.c.) three or four times daily, has for many years been freely used. It should be noted, however, that this mixture has no direct curative influence on the renal condition, is not diuretic, and should be used only with the purpose of overcoming anemia. In cases that are not anemic, iron is likely to do more harm than good owing to its tendency to lock up the bowels. In **chronic parenchymatous nephritis**, the form in which iron is most useful, it is a good plan to determine the proper dose by examination of the stools; if these are decidedly blackened, too much is being given. In chronic interstitial nephritis and acute forms of nephritis, iron is rarely, if ever, indicated, though during convalescence after **acute nephritis** it

is often of considerable value. Tincture of ferric chloride may be given instead of Basham's mixture if desired.

In **erysipelas** iron has been credited by some with almost specific properties, though others have failed to obtain corresponding results. The plan generally followed is to give large doses of the tincture of ferric chloride (10 to 60 minims—0.6 to 4 c.c.), well diluted, every four hours. Salicylate of iron has in late years, however, found much favor as a substitute for the tincture.

Mixture of the tincture of perchloride of iron and sodium salicylate recommended for **erysipelas**, **acute tonsillitis**, in some cases of **croupous pneumonia**, **puerperal sepsis**, **sublingual adenitis**, **rheumatic endocarditis** with hyperpyrexia, etc. It acts as a powerful febrifuge even in small doses and does not produce diaphoresis.

Among 50 cases of erysipelas, none lasted for more than forty-eight hours after the commencement of the administration, and the headache and general malaise disappeared at the end of eight hours; the only supplementary medical treatment was an evening dose of 1 to 2 grains (0.06 to 0.12 Gm.) of calomel or a saline morning aperient. The mixture employed was made up by dissolving 1 dram (4 Gm.) of sodium salicylate in 2 ounces (60 c.c.) of water, which was added to 2 drams (8 c.c.) of tincture of ferric chloride; potassium chlorate, $\frac{1}{2}$ dram (2 c.c.); glycerin, $\frac{1}{2}$ ounce (15 c.c.), and water, to 3 ounces (90 c.c.). The whole was made up to 8 ounces (240 c.c.), the dose being 2 tablespoonfuls every three or four hours. In acute tonsillitis resolution and cure occurred generally in twenty-four to forty-eight hours, and even in cases where suppuration had occurred the pus was rapidly absorbed. Along with the internal use of the salicylate of iron the author employed a gargle of iodine solution, $7\frac{1}{2}$ to 30 minims (0.45 to 1.8 c.c.) of tincture of iodine

to the pint of water, used four-hourly. It is inadvisable to continue the use of the iodine preparation for the throat or nose longer than three days, as it may produce an inflammatory condition (which a weak alum sulphate solution will relieve). F. J. Gray (Edinburgh Med. Jour., Nov., 1905).

In **diphtheria** the tincture of the chloride has been used, both internally and locally, with asserted marked benefit, especially as a systemic "supportive." Whitla considers iron of special value in cases complicated with streptococcic or other septic infection, and refers to the following as a good formula, suitable for a child about 4 years of age:—

R *Tinctura ferri*

chloridi f3j (4 c.c.).

Potassii chloratis.. gr. xxxv (2 Gm.).

Glycerini f3vj (24 c.c.).

Aqua chloroformi,

q. s. ad f3iv (120 c.c.).

M. Sig.: Dessertspoonful every four hours.

Quinine or strychnine might likewise be combined with the iron. The use of potassium chlorate is by some objected to on the ground that it induces degenerative changes in the renal tissue.

Attention called to the great value of perchloride of iron in **blood-poisoning, erysipelas, scarlet fever, diphtheria**, etc. Its beneficial effects are ascribed by the author to the presence of free chlorine. The remedy must be carefully used; large doses not infrequently increase fever and set up intestinal irritation, palpitation, and headache. Latham (Lancet, Nov. 19, 1904).

In **epilepsy** and **chorea** in weak, anemic subjects the use of ferrous bromide in doses of 5 to 20 grains (0.3 to 1.3 Gm.) has been recommended. Hecquet reported that of 25 cases of **spermatorrhea** treated with 3- to 5- grain

(0.2 to 0.3 Gm.) doses of ferric bromide, only 2 were unrelieved.

Ricord termed the tartrate of iron and potassium "the born enemy of **phagedena**," and used it both internally and locally in this complication of **chancroid**.

Local Uses.—The strong astringent properties of some of the iron salts render them highly efficient as styptics. Monsel's solution (*Liquor ferri subsulphatis*) and the official aqueous solution of ferric chloride (*Liquor ferri chloridi*) are the preparations chiefly used. In **gastric hemorrhage** 1 to 5 minims of the former solution, diluted in ice-water and repeated as required, will generally be followed by relief. In **epistaxis** a weak dilution of Monsel's solution (f5j-f3viii—4-240 c.c.) has been advised, to be used in the form of a spray.

The disadvantage as styptics of the iron salts in common use is that they are caustic, owing to the free acid radical (chloride or sulphate) left upon combination of the iron with the tissues. These salts tend to cause the formation of a superficial slough or eschar and should therefore never be applied for hemostatic purposes to aseptic wounds, especially since the dense, adherent clot formed by the iron offers an excellent nidus for the lodgment and reproduction of bacteria. The obstruction formed by iron to the outflow of blood is not a true clot, as it contains no fibrin and consists merely of iron albuminate which blocks up the open vessels. This being the case, iron salts are powerless to control hemorrhage unless they can be brought directly to the bleeding point.

Ferripyrin, a combination of iron with antipyrin, has been recommended as being free from the caustic effects of

the other salts, while preserving the hemostatic properties of each of its constituents. Either the powder or a 20 per cent. solution of this drug may be applied; in the latter case cotton tampons are saturated with the solution and applied to the bleeding surface. **Epi-staxis**, among other conditions, has been relieved by the introduction of small tampons soaked in ferripyrin (Hedderich).

In **intestinal hemorrhage** iron is usually of but little utility, as it probably becomes converted into the inert sulphide during its descent in the alimentary canal. The administration of hard pills containing 3 grains (0.2 Gm.) of iron subsulphate has, however, been advised. In bleeding **hemorrhoids** the loss of blood may be diminished or even arrested by washing the protruding masses with Monsel's solution. The tumors should be well oiled before they are returned. Iron in the form of Monsel's salt (ferric subsulphate) can likewise be added to the antipruritic and astringent ointments frequently prescribed for hemorrhoids, where the bleeding persists notwithstanding the use of other drugs.

A combination of the perchlorides of iron and mercury constitutes an efficient intestinal antiseptic. Fifteen minims (1 c.c.) each of *liquor hydrargyri perchloridi* (B. P.; 0.1 per cent. HgCl_2) and *tinctura ferri chloridi*, combined with a little glycerin and chloroform water, give good results in **typhoid fever**, in **acute** and **subacute colitis**, especially when ulcerative, and in **dysentery**. It should be kept in mind that combination with albumin or alkalies destroys the antiseptic action. T. S. Wilson (Brit. Med. Jour., Feb. 16, 1924).

Hemorrhage following **leech-bites** and **tooth extraction** can readily be arrested with Monsel's solution.

Internal use of iron to arrest hemorrhage in parts of the organism other than the alimentary tract, *e.g.*, in **metrorrhagia**, **hemorrhage post abortum**, **purpura**, **hemophilia**, etc., has been advocated, but is not likely to prove efficient unless anemia underlies the hemorrhagic manifestations. In **hemoglobinuria** Baccelli has found the administration of iron subsulphate, in conjunction with oxygen inhalations and hygienic measures, most useful.

The astringent properties of iron are availed of for purposes other than arrest of hemorrhage in, *e.g.*, **diphtheria**, in which Monsel's solution may be applied to the tonsils and pharynx, either pure or diluted with 2 or 3 parts of glycerin, to constrict the tissues and limit extension of the exudate. In **follicular tonsillitis** and in **pharyngitis** the same procedure gives gratifying results, though some degree of pain may follow the application.

Fissured nipples can be caused to heal by brushing with Monsel's solution diluted with 3 parts of glycerin. The undiluted solution will cause **syphilitic vegetations of the glans and prepuce** to disappear. Ferripyrin in 1 to $1\frac{1}{2}$ per cent. solution has been recommended by Hedderich as an astringent injection in **gonococcal urethritis**.

Roundworms (ascarides) can be removed by injections of a weak dilution of the tincture of ferric chloride.

The use of freshly precipitated ferric hydroxide as an antidote in **arsenic poisoning** was mentioned in the section on PREPARATIONS AND DOSE.

C. E. DE M. SAJOUS

AND

L. T. DE M. SAJOUS,
Philadelphia.

IVY POISONING. See **DERMATITIS VENENATA**.

JALAP.—Jalap (*Jalapa*, U. S. P.), named from Jalapa, a city of Mexico, is the dried tuberous root of *Exogonium Jalapa* (*Exogonium purga* or *Ipomœa purga*), a vine of the family Convolvulacæ, indigenous to Mexico, and also grown in Jamaica and India:

The active principle of jalap is a resin, present in amounts varying from 8 to 12 per cent., and which contains the two purgative glucosides, *convolvulin*, or *jalapurgin*, and *jalapin*, the latter considered identical with scammonin.

PREPARATIONS AND DOSE.—*Jalapa*, U. S. P. (jalap), required to contain not less than 7 per cent. of the total resins of jalap. Dose, 15 grains (1 Gm.).

Resina jalapæ, U. S. P. (resin of jalap), consisting of yellow to brown masses or a powder, with somewhat acrid taste, insoluble in water and oils, but soluble in alcohol. Dose, 2 grains (0.125 Gm.).

Pulvis jalapæ compositus, U. S. P. (compound jalap powder), consisting of jalap, 35 parts, and potassium bitartrate, 65 parts. Dose, 30 grains (2 Gm.).

Fluidextractum jalapæ, N. F. (fluidextract of jalap). Dose, 15 minims (1 c.c.).

Tinctura jalapæ, N. F. (tincture of jalap), 20 per cent. Dose, 1 fluidram (4 c.c.).

Tinctura jalapæ composita, N. F. (compound tincture of jalap), each fluidram (4 c.c.) of which represents $7\frac{1}{2}$ grains (0.5 Gm.) of jalap and $1\frac{3}{4}$ grains (0.12 Gm.) of resin of ipomœa. Dose, 1 fluidram (4 c.c.).

Jalap is also contained in the *Pilula hydrargyri chloridi mitis compositæ* (U. S. P.) and *Pilula cathartica vegetabiles* (N. F.), for the composition of which see COLOCYNTH.

PHYSIOLOGICAL ACTION.—Jalap acts as a powerful hydragogue cathartic. Gastrointestinal irritation is produced by excessive doses. It is also irritating to other mucous membranes, e.g., when snuffed into the nostrils as a fine powder. The resin was detected by Müller in the blood of dogs given jalap, but cannot be found in the urine or feces, and is therefore believed to be oxidized in the body. Jalap passes into the milk, and purges nurslings.

POISONING.—Jalap when taken in overdose causes, in addition to copious

watery stools, tormina and tenesmus, at times accompanied by nausea and vomiting. The treatment consists in evacuation of the retained jalap with the stomach-tube and the use of demulcent drinks.

THERAPEUTICS.—Jalap is used principally to relieve dropsical effusions, **anasarca**, and **ascites** in cases of **heart disease**, **nephritis** or **hepatic cirrhosis**. The resin is almost tasteless, and, the dose being small, may be given to children in doses of $\frac{1}{4}$ to $\frac{1}{2}$ grain (0.015 to 0.03 Gm.). The maximum dose for adults is $7\frac{1}{2}$ grains (0.5 Gm.). According to Debove and Pouchet, the resin is less effective than powdered jalap, given with honey. The preparation most frequently used, however, is the compound jalap powder, which possesses some diuretic power in addition to its property of causing copious watery bowel evacuations. If necessary, it may be given daily for some time without harm. In **pulmonary congestion** and **distended right heart** with cyanosis and dyspnea (so-called "**cardiac asthma**"), a teaspoonful of compound jalap powder will give relief. In **acute fibrinous pleurisy** $\frac{1}{2}$ to 1 dram (2 to 4 Gm.) of the same preparation may be advantageously given at bedtime to overcome abdominal distention and the resulting dyspnea (Capps). In **hemorrhoids** it does not cause irritation, but, on the contrary, brings relief by emptying the vessels above and clearing out the liver. As an active purge where the liver is torpid, jalap with calomel is very active. In **cerebral hyperemia** the hydragogue action of jalap is also useful.

Jalap acts generally in two to four hours.

JAMBUL.—Jambul is an East Indian tree of the family Myrtacæ. It is the *Syzygium jambolana* of de Candolle. From the fruits, by alcoholic fermentation, a liquor is obtained, the *jambava* of the Hindoos.

PREPARATIONS AND DOSE.—Jambul is not official. The preparation generally employed is a powder made from the bark, or, better, from the seeds, given in doses of 5 to 60 grains (0.3 to 4 Gm.). A fluidextract made from the seeds is more conveniently administered, in graded

doses of from 10 to 30 minims (0.6 to 2 c.c.). A fluidextract of the bark has also been used by Vix in doses of 1 to 5 fluidrams (4 to 20 c.c.) several times a day, as well as the whole fruit, preserved in alcohol. The pulp of the dried fruit is not considered of any value.

PHYSIOLOGICAL ACTION.—Jambul acts as a gastric tonic, but the property for which it has been most employed is that of diminishing glycosuria. Groeser gave dogs phloridzin and an extract of jambul, and found that the sugar was invariably diminished almost to $\frac{1}{2}$ that excreted under the action of phloridzin alone, and the duration of the glycosuria considerably lessened.

THERAPEUTICS.—Jambul has been especially extolled in **diabetes mellitus**, but, on the whole, has given but a moderate degree of success, chiefly in cases of a mild type. The drug has also been used in **diabetes insipidus**, with asserted benefit. It should be taken after meals; otherwise, in sensitive patients, nausea may be produced.

JAPANESE RIVER FEVER, OR SHIMA MUSHI.—This disease, also known as "flood fever," occurs in the hemp districts on the banks of two rivers of Japan, the Shinanogawa and Omonagawa. It is ascribed to the bite of the Kedani larval mite, resembling, morphologically at least, *Leptus autumnalis*. The bite is followed by an eschar, which ulcerates and then gives rise to fever, an exanthematous eruption, lymphangitis, conjunctivitis, and bronchitis. It ends fatally in about 15 per cent. of the cases.

TREATMENT.—The disease is prevented by avoiding the districts to which it seems to be restricted, but if traveling in the infected hemp countries is necessary, strict personal cleanliness aids greatly to prevent infection. The only remedial measures which have shown any value are **sodium salicylate** and **quinine**, preferably the **hydrochloride**. Locally, **iodine ointment** upon the bites or under the eschars is sometimes useful. The general phenomena and complications call for appropriate measures. (See **CONJUNCTIVA**, **BRONCHITIS**, etc.)

JAUNDICE. See **LIVER, DISEASES OF.**

JEQUIRITY.—Jequirity is the name given in Brazil to the seeds of the *Abrus precatorius*, or wild licorice, a climbing shrub of the family Leguminosæ, indigenous to India, but now naturalized elsewhere in the tropics. The seeds, or beans (prayer beads; crab's eyes; jumble beads), are about $\frac{1}{8}$ inch in diameter, nearly spherical, bright-red, with a black spot at the hilum, inodorous, and with a slight bean-like taste. In India they are employed as a weight standard (about $1\frac{1}{2}$ grains). Though inert when taken whole into the stomach (Warden and Waddell), the seeds contain a protein active principle, *abrin*, closely resembling snake-venom in action.

PHYSIOLOGICAL ACTION.—The poisonous and irritant properties of jequirity are due to the contained abrin, which has been termed a "vegetable agglutinin" and is a powerful cardiac depressant. Roemer found that the dose of abrin required to kill a mouse was but 1 two-millionth of the body weight.

Ehrlich observed that animals could be immunized to abrin. Roemer showed that repeated instillations in a rabbit's eye will produce a marked local immunity, soon followed by general immunity. Calmette and Deléarde prepared an effective anti-abrinic serum.

POISONING.—While pounding jequirity seeds one is liable to an attack of conjunctivitis, rhinitis, or bronchitis, and any cuts or scratches on the fingers become swollen and painful. Careless handling of abrin is extremely dangerous to the eye and the nose. The smallest particle may be fatal in the slightest wound, $\frac{1}{100}$ grain (0.00065 Gm.) of abrin being a lethal dose for a man of 130 pounds weight. The symptoms are faintness, vertigo and vomiting; cold, clammy surface; dyspnea; a small, frequent, irregular pulse; convulsions, collapse and death.

Treatment of Poisoning.—Cardiac stimulants should be exhibited and external warmth applied. Amyl nitrite might prove of value. As a specific measure, **jequiritol serum** should be injected subcutaneously or applied locally, according to indications.

THERAPEUTICS.—In this country the use of jequirity is limited to obstinate cases of *trachoma* and *pannus*, especially the latter. The essence of its action consists in the replacement of an existing chronic inflammation by another of more violent type, but of limited duration. De Wecker recommends its use as follows: Powder 32 jequirity berries and macerate for 24 hours in 1 pint ($\frac{1}{2}$ liter) of cold water; add an equal quantity of hot water, and filter when cool. Sattler advises that the husks of the seeds be removed by means of hot water before the infusion is made. The seeds are then powdered and 6 fluidounces (200 c.c.) of hot water added. After standing for 24 hours, the infusion is filtered. The solution should be freshly made before use, as it decomposes very quickly.

Painting of the infusion on the conjunctival surface of the eyelid with a brush is followed by an acute diphtheroid inflammation, lasting three or four days, and attended with fever and pain in the eyes and frontal region. This so changes the chronic process present as to permit of a cure. If an excessive action is developed, it may be controlled by hot compresses of a very dilute solution of corrosive sublimate (Ilaire), or, better, by frequent instillation of jequiritol serum. If the first application causes but slight reaction, it may be repeated after 24 hours, and so on until the desired reaction is obtained.

An improved preparation is that known as *jequiritol*, introduced by Roemer. It is a sterile liquid containing 50 per cent. of glycerin, and abrin in 4 different but definite strengths. A single drop of No. 1 is first instilled, then an increasing number of drops, until the characteristic jequirity inflammation is seen. In a few cases No. 1 will produce no reaction, and No. 2 is then used. Upon repeated courses of treatment an immunity develops, so that even No. 4 will cause no reaction. Whenever too violent a reaction occurs it may be overcome by dropping into the eye at short intervals a few drops of Roemer's *jequiritol serum*.

In the presence of purulent conjunctivitis or keratitis, fresh trachomatous pannus, recent opacities, or diseases of the lachrymal apparatus, jequirity is contraindicated.

JOINTS, DISEASES OF.—The two dominating general disorders of this series, *arthritis deformans* and *atrophic arthritis*, were reviewed under the general heading of *ARTHRITIS* in the second volume. Under the present heading, the medico-surgical forms with which every physician should be thoroughly familiar to avoid diagnostic errors, such as *septic arthritis*, *synovitis*, *Charcot's tabetic arthropathy*, *Köhler's disease*, *Bertolotti's syndrome*, *tuberculous arthritis*, *Poncet's tuberculous arthritis*, and *syphilis of the bones and joints* will be considered.

In some of these disorders, my researches in the relationship between the endocrin organs and pathology warranted a brief reference to the pathogenic rôle of these organs. This was deemed advisable in view of the fact that this departure will tend to elucidate questions which have remained obscure.

SEPTIC ARTHRITIS.

SYNONYM.—*Infective Arthritis*.

DEFINITION.—Septic arthritis is due to invasion of the joints by pathogenic organisms in the course of general or local infections. These initiate and sustain a defensive process in which the arthrodial tissues are more or less subjected to autolysis by enzymes rendered abnormally active through endocrin hyperthermogenesis. (Author's definition.)

SYMPTOMS.—In the absence of suppuration the symptoms, which greatly resemble those of rheumatism, are very similar whichever be the causal germ, although the periods of incubation may differ. The joint becomes the seat of an effusion, usually with pain. Occasionally but one joint is affected. When such is the

case the joint is apt to be a large one, *e.g.*, the knee or hip. This is frequently true in puerperal, typhoid, and other fevers. In pyemia several joints are apt to be attacked.

The onset is likely to be very insidious, and may pass unnoticed at first, being masked by the symptoms of the general affection. The pain in the joint may produce a restlessness which is usually attributed to nervous or other disturbances, so that the disease may be far advanced when recognized.

Sometimes the local disease progresses with great rapidity, pus being present in the joint almost from the first. The joint swells and becomes the seat of an effusion. Elsewhere in the body, however, pain may be the earliest symptom, occurring, in fact, before any definite sign of joint disease appears. The color of the skin over the joint is not apt to be changed at first; but if disorganization of the joint takes place, it may become red and edematous.

In the hip-joint, which is exceedingly liable to involvement in typhoid fever, dislocation is very apt to occur. If the hip trouble occurs early in the course of the general disease, it may be difficult to differentiate the condition from acute hip disease of tuberculous nature. It may also simulate displacement of the hip. It can be distinguished from rheumatism, especially when located in the knee-joint or elbow, by the fact that it does not migrate.

Oftentimes, if the general disease tends toward recovery, the local joint trouble may be more of the nature of a synovitis than an arthritis, and may pursue a mild course, particularly if only a single joint is affected. If,

however, the general disease is grave, the local disease is of a purulent character almost from the start, and suppuration may persist a long time, until death occurs.

Value of bacteriologic examination in all cases of arthritis not obviously of rheumatic origin emphasized. While *pneumococcus* arthritis occurs oftenest in children, the writer's case was in a man of 25 and appeared solely in the left knee 3 weeks after recovery from a severe diarrhea. In 2 weeks there was marked fluctuation, and flaky yellow fluid containing pneumococci was obtained. Under subcutaneous injections of **antipneumococcus serum** rapid improvement occurred and the next puncture showed absence of pneumococci. **Extension** of the limb with weights gave much relief from pain. The case would probably have ended fatally had its pneumococcic nature not been discovered. Grubb (Brit. Med. Jour., Sept. 13, 1924).

Pneumococcus arthritis is generally postpneumonic, but it may also follow extrapulmonary localization of lesions due to the pneumococcus. *Pneumococcus* arthritis involves most commonly the larger joints, and is apt to be monoarticular. The onset of such arthritis is usually sudden and is accompanied by mild general discomfort and local pain and swelling. *Pneumococcus* arthritis may assume any one of 3 different forms: (1) Rheumatoid, of mild symptomatology and short duration; (2) serous, rather infrequent and passing spontaneously, running a mild course; (3) suppurative, the commonest form. The prognosis is rather good. Favorable results are enhanced by early diagnosis and appropriate treatment. Good therapeutic effects frequently follow **puncture and evacuation of the joint**, combined with **immobilization and vaccine therapy**. G. Taccone (Pediat., Oct. 15, 1924).

PATHOLOGY AND PATHOGENESIS.—In most instances septic arthritis is polyarticular if the infec-

tion is a general one due to or originating in a focal infection; but an infective process close to a joint, or a wound reaching the latter, may cause a monarticular arthritis. The latter may, nevertheless, result in a general arthritis, as the bacteria are transmitted by the blood and lymph channels.

To enumerate the diseases due to pathogenic organisms which thus cause infective arthritis is unnecessary, since any infection, general or local, may initiate it. The time it takes for such a complication to occur varies greatly, however, for while typhoid fever may become complicated with arthritis only several days or even weeks after the onset of the active febrile symptoms, a streptococcic infection, *e.g.*, that due to erysipelas, may induce arthritis within a very few days, indeed almost at once. The arthritic complication may itself give rise to pneumonia, through conversion, according to Rosenau, of streptococci into pneumococci.

As I have urged elsewhere, the pathogenic organisms or toxins themselves are not the direct factors in the development of the arthritis, as is now generally believed, but, instead, the defensive process which aims to destroy the germs and their toxins. Briefly, the defensive enzymes subject to proteolysis and hydrolysis not only the various pathogenic agents themselves, but also the tissues of the affected joints. Hence the fact that even in acute cases the contents of the joints present various kinds of detritus. Thus, an acute joint may show no bacteria, so rapidly has the defensive process controlled the local infection, but only a sanious fluid. This is illustrated by the presence of pyogenic bacteria and pus composed

of phagocytes gorged with them, and other detritus, in the aspirated fluid.

TREATMENT.—Formerly the aim was to “soothe the irritation of the joint and protect it.” Time has shown, however, that such a course only favors the destructive process. The growing tendency has been toward active measures calculated to eliminate the pathogenic factors of all kinds, bacteria, their toxins, etc., from the joint. Most surgeons, therefore, resort to **aspiration** of the fluid, and if it is found to contain streptococci, staphylococci, gonococci, or other pathogenic organisms, the joint is **irrigated**, first with **sterile salt solution**, then with some active bactericidal agent—a solution of **boric acid** in mild cases, and in the more severe, a weak one of **mercury bichloride** (1:15,000), a 2 to 5 per cent. **phenol** solution, or the Murphy solution of **formalin**, 2 per cent. in glycerin, at least 24 hours old, which, though painful, and therefore requiring a general anesthetic, such as **nitrous oxide-oxygen**, is regarded as the most effective.

In knee cases, Mayo-Robson recommends **drainage**—not, however, with the limb in the usual position, which causes the septic contents of the joint to burrow backward into the popliteal space or along the course of the tendons in that region, upward into the thigh and downward into the leg, or in both directions. The aim should be, instead, to make the suprapatellar pouch dependent. This may be accomplished by placing the limb in a position at right angles to the body, with the patient in dorsal decubitus, or by raising the foot of the bed with the body in the prone position. By merely inserting a tube into the top of the pouch, the whole joint can

thus be completely evacuated and purified, and if this is done sufficiently early, a speedy recovery may be anticipated, with the joint's mobility unimpaired.

It is generally recommended that the drainage tube extend only to the capsule and not into the joint. Each joint requires, to obtain the best results, a position which will enable it easily to evacuate its septic contents. The joint should then be **immobilized** to insure physiological rest until the wound is healed. Later, gentle **passive motion** and **massage** will assist recovery if done with due care; any violent movement or forcible handling of the muscles, on the other hand, may cause resumption of the attack.

If, despite all these measures, the case persist, or if it be severe, the joint should be opened, *i.e.*, subjected to **arthrotomy**, and **irrigated with saline solution**. If pus be found in the fluid withdrawn, **Dakin's solution** should be used.

An important feature of the whole treatment is the removal, where possible, of any source of infection, wherever located. **Autogenous vaccines**, the **toxins of erysipelas**, **bacillus prodigiosus** and others, have been recommended by some authors, but found ineffectual by others. A severe reaction should, however, be avoided under any circumstances.

SYNOVITIS.

DEFINITION.—The term synovitis denotes an inflammation of the synovial membrane—a fine connective tissue layer which lines the joints, excepting their cartilaginous articular surfaces, and insinuates itself into the interstices between the bones and ligaments.

SYMPTOMS.—Pain, heat, redness and swelling with impairment of function are the leading symptoms, but these vary according to the duration of the disease and the nature of the morbid changes that have occurred. The detailed symptoms, as given below, are in the words of my regretted friend and predecessor in this department, Professor Gwilym G. Davis.

Acute Synovitis.—In acute synovitis the pain may vary from slight to excessively severe. The rapidity with which the effusion may occur can cause intense pain through distention of the joint-capsule. The joint may be red and hot to the touch and very tender. The swelling is due mainly to distention of the joint, both by the increase in size of the synovial fringes and by the increased effusion. Swelling is a most important symptom, and it is much more marked in some cases than in others. In such joints, *e.g.*, the knee, as are not deeply covered by soft parts, the swelling is marked and peculiar in shape, while in those which are not so superficial, as the shoulder and hip, it may be so slight as not to be evident. In these latter joints there may be a slight uniform enlargement which it would be difficult to say was not due to the bruising of the soft parts in case the affection followed an injury. In the knee and ankle, on the contrary, the swelling may be marked, and follow accurately the outlines of the joints. It is influenced in its shape by the overlying structures. Thus, in the knee-joint the swelling of the synovial fringes below the patella causes a protrusion at that level, which is more marked on each side of the tendo patellæ. There may be a swelling above the patella or on

each side. The patella is likewise lifted up away from the femur by the effusion, forming the so-called "floating patella," or, upon pushing the patella downward, it can be felt to strike against the condyles beneath. When the subfemoral bursa communicates with the joint, the swelling often extends quite a distance above the patella. In the ankle-joint the swelling is situated more toward the sides, but is also seen in front. Behind, it is not so marked, except on each side of the tendo Achillis, which, however, does not play so prominent a part among the symptoms of affections of this joint as do the patella and its tendon in those of the knee. In the case of the elbow, the tendon of the triceps muscle also causes the swelling to be greater on each side than in the middle.

Impairment of function in synovitis is usually marked, and movements are very painful in the acute type of the affection. Not only does pain interfere with the joint's functions, but the effusion into and distention of the joint prevent it from performing them by rendering it looser and less secure, so that weakness is pronounced and, even if pain be absent, the joint is practically useless.

When an acute synovitis is produced by traumatism only, the effusion is serous, and in a healthy individual it is apt to remain so. After appropriate treatment it will usually disappear, but if at the time of the reception of the injury infection is introduced, then pus is likely to form within the joint, and unless radical measures are at once instituted, disorganization of the joint and even general infection and death may occur. In other cases the injury serves

as a "*locus minoris resistentiæ*," or place of weakened resistance; the effusion seems to become infected from the blood, and soon may assume a purulent character. In still other cases the synovia seems to be infected from the start, and, while the effusion may be serous at first, it rapidly becomes purulent. In these there may or may not be a history of traumatism. Cases accompanying or following the infectious fevers,—typhoid, pneumonia, and others,—as well as those arising from previously existing pyogenic infections, such as appendicitis, infected wounds, etc., are of this character.

Subacute Synovitis.—In subacute synovitis the symptoms may be less abrupt in their onset and less violent in character. An acute attack may be slow in subsiding or the affection may be mild from the start. The heat, pain, and redness are not so marked as in the acute type.

Chronic Synovitis.—In chronic synovitis the symptoms are characterized by their persistence. The acute pain gives way to a dull, persistent pain, aggravated by use of the joint to such an extent as to forbid it entirely. The redness may disappear and the heat may only slightly or not at all exceed that of the opposite side, but the swelling usually remains and forms a most prominent symptom. The swelling of the synovial membrane of the joint may overshadow the effusion, and then the joint has a boggy or doughy feel which is highly characteristic. The swelling may be very great, owing to the large amount of effusion.

Effusion of lymph is most apt to occur in the violent inflammations of acute attacks. Pus does not often oc-

cur in cases of simple synovitis, because infection is lacking. Should this, however, from any cause take place, then pus forms quickly enough.

The existence of chronic synovitis implies disuse of the affected member for a considerable time. Marked trophic changes therefore occur. The muscles above and below the joint atrophy, while the joint remains swollen, each of these changes tending to aggravate the appearance of the others, so that together they form a picture of helplessness which is amply borne out by the total inability of the patient to use the joint. If a joint of the lower extremity is affected, the patient either is compelled to refrain from walking or hobbles about only with the greatest difficulty, while if the upper extremity is involved the arm is usually carried in a sling.

ETIOLOGY.—The principal cause of simple synovitis is injury. The joint may have been knocked, bruised, or strained. Exposure to cold and wet may be followed by a simple inflammation of a joint, with no other evidences of rheumatic or other constitutional affection. Sometimes the disease seems to appear without immediate cause, but in these cases the affection has probably been the result of an injury so slight as not to have attracted the attention of the patient at the time or else have been since forgotten.

If infection is introduced either at the time of the injury or subsequently through the blood-stream, the effusion rapidly becomes purulent. Cases arising without any history of previous injury are almost certain to have an infectious origin. They may be metastatic in character and may also be due to syphilis, gonorrhea,

etc., although the effusion present in a synovitis due to the last-named cause is more apt to be of a plastic than of a fluid character. Focal infections, particularly when located in the teeth, tonsils and sinuses, have also been incriminated.

PATHOLOGY.—The affection consists of an inflammation of the synovial membrane of the joint with an outpouring of synovia, serum, lymph, or pus into the joint-cavity.

In health the synovial membrane is clear, shiny, thin, and more or less transparent, but when inflamed it becomes dull, dark red in color, and is much swollen and thickened. It is this thickening of the synovial membrane that so often produces the swelling which is seen across the front of the knee-joint at the level of the lower edge of the patella. It is also the main cause of the swelling in diseased joints where no free fluid can be demonstrated. The synovial membrane is extremely vascular, and when irritated pours serous fluid into the joint and later even pus, and may serve as the point of origin of loose or floating bodies.

The joint-surfaces may lose to some extent their smooth, glistening character, while the synovial fringes become injected, begin to proliferate, and tend to encroach on the interior of the joint and the surrounding cartilage. The natural secretion of the joint may become increased; it may contain lymph or even pus. In a quickly developing synovitis the secretion may be thinner than normal, owing to the sudden outpouring of serum. Not infrequently the injury which has produced the synovitis may likewise have caused some bleeding into the joint, in which case the con-

tained fluid will be blood-stained or even consist of blood-clots.

While the first effusion may be liquid in character, it may speedily disappear and leave a fibrinous effusion, with enlargement of the synovial fringes. The latter gradually solidify and form adhesions, which tend to bind the bones together, producing a fibrous ankylosis that limits movements and seriously cripples the joint.

TREATMENT.—The treatment of synovitis varies with its acuteness. In a sharp attack constitutional disturbance may be marked, the pain is severe and fever high, and the patient is tortured by suffering and deprived of sleep. A free **saline purge** is of service, aided by **acetanilide** or **acetphenetidin**. To produce sleep **sulphonal**, **trional**, or **barbital** may suffice. If there is severe pain, **Dover's powder** or other opiate becomes necessary. Recently, however, the aim has been to forestall infection of the joint by promptly and repeatedly aspirating it under strict antiseptic precautions, watching carefully for any symptom of infection.

Even in acute traumatic synovitis the writer resorts to **repeated aspirations**, with **active motions** and **walking without splints**. When aspiration is employed promptly it relieves the pain and prevents stretching of the ligaments. Last but not least, cure is obtained in $\frac{1}{2}$ of the time required by the immobilization treatment. McWilliams (*Annals of Surg.*, Dec., 1922).

Advocating **aspiration** many years ago for the removal of effusion to prevent its conversion into a purulent one, Davis never had the slightest bad effects from it when the following technique was employed: "Properly to tap a joint, the first essential is to get a sharp trocar the cannula

of which is so closely fitted as to allow it to pass through a piece of leather without catching. Very few trocars stand this test, and all others are positively dangerous. It should be thoroughly disinfected—preferably by boiling. The part should be likewise thoroughly cleansed by scrubbing and antiseptics, or by painting with iodine, as for any other serious surgical operation. The surgeon's hands require the same careful treatment. After tapping, the opening should preferably be sealed with collodion and gauze or cotton. If a bandage is applied with a dressing, the greatest care should be taken that it be so large and so firmly secured that it can by no possibility become displaced and the puncture exposed."

Most writers are dissatisfied with the ordinary methods used, and advise more active treatment, such as **early aspiration** of all cases of severe synovitis, as well as better **fixation** during the first period while the patient is recumbent, more prolonged treatment during convalescence, and early and increasing **massage** and **motion without undue strain**. Dresel (*Cal. and West. Med.*, Mar., 1924).

Cases deprived of this early protective measure are still encountered in practice, and violent infection with suppuration may be found present. **Lateral incisions** are then made under ether, the pus is evacuated under strict antiseptic precautions, and **no drains** are inserted. If a joint in an extremity be affected, **active motion** is begun as soon as the patient recovers from the ether, and is repeated every 2 hours; if the involved member be a leg, walking should be resumed in 48 hours. If evidences of infection persist, the foci should be sought, evacuated, and the joint

washed out through the same cannula. Antiseptics, such as **mercury bichloride**, 1:5000, or **phenol**, 1 per cent., may be used, but they are not to be allowed to remain in the joint. The surest procedure is Murphy's method, which consists in injecting after aspiration of the joint a 2 per cent. **formalin solution in glycerin**, freshly prepared. This causes so much pain, however, that **general anesthesia** is sometimes necessary.

In *chronic synovitis*, without infection or marked pain, persistent, but not violent **passive motion** and **massage** are indicated, together with **dry heat**. If this is not successful, free movement of the joint under an anesthetic may be tried, followed for a short time by complete **rest** and the **ice-cap**, if there is pain, until reaction is past, when **passive movements** and **massage**, the use of the **hot-air bath**, the application, perhaps, of **iodine** to the joint, or compression by a **rubber bandage** may be resorted to. Or, **rest** and compression may be secured by means of a **plaster-of-Paris dressing**. The **Bier treatment** is also advocated by some surgeons.

Here, as in the acute form of synovitis, **aspiration** of the joint, followed by irrigation with **warm saline solution** and the injection either of one of the ordinary **antiseptic solutions** mentioned above, or of the **Murphy solution**, is being increasingly advocated. Particularly is such treatment desirable when hydrarthrosis invalidates the patient.

CHARCOT'S TABETIC ARTHROPATHY.

SYNONYMS.—*Charcot's disease*; the *Charcot joint*; *neuropathic arthropathy*.

DEFINITION.—This joint disorder, which occurs sometimes as a complication of locomotor ataxia, is due to autolytic lesions in the spinal cord which inhibit more or less the functions of the nerve paths that govern the arterial supply of the joint affected and thus arrest correspondingly its nutrition and cause its disintegration. (Author's definition.)

SYMPTOMS.—As pointed out by Raymond, the arthropathy may be the only sign of locomotor ataxia, occurring at times during the initial stage of this disease. In a few hours the joint may become enlarged to twice its normal size. Subcutaneous edema appears, the synovial secretion rapidly distends the synovial sac, bursts this, and then infiltrates the neighboring parts. The articular cartilages and adjacent bony parts undergo either atrophic or hypertrophic changes. Sometimes the joint swelling subsides and does not reappear; at others, it subsides but reappears; at others still, it remains in a chronic condition.

Swelling of the joint is often very great. The character of the pain, which is present only to any marked degree in the early stages and is replaced later by anesthesia, serves to distinguish Charcot's disease from true osteoarthritis, in which the suffering is severe and continuous. Again, whereas the affected joint in the latter tends to ankylose, in Charcot's disease it is flail-like. The disorder usually attacks single joints, but both knees or both elbows, or an elbow and fingers, may be affected. There is usually no constitutional involvement.

As stated by Llewellys F. Barker, any joint is susceptible to involvement, but the

larger ones more than the smaller. Two special forms are the *tabetic foot*, in which the bones of the arch are particularly involved, and the *tabetic spine*, differing from other types of spondylitis deformans in the sudden onset, extensive destruction of the parts, and the associated tabetic symptoms. The joint lesions of syringomyelia are very similar to those of tabes, but the common occurrence of pain, the predominance of involvement of the upper extremities (80 per cent. of the cases), and the longer course of the affection are notable differences.

Such a case is often puzzling to the clinician. Whenever an adult patient comes with a joint largely distended with fluid, with comparatively slight pain, and with symptoms apparently too mild for the evident destructive lesions present, one should search for ataxic symptoms. When the typical signs of tabes, the belt pains, gastric crises, etc., are present, the diagnosis is easy.

Case of Charcot's disease in which the left knee became swollen and painful as the first and long the only manifestation of tabes. There was no history of syphilis, and a negative Wassermann reaction, but a trophic lesion was evident on the right foot, and the X-rays revealed syphilitic changes in the periosteum. Cunha and Estapé (Anales de la Fac. de Med. de Montevideo, Dec., 1924).

PATHOLOGY AND PATHOGENESIS.—The changes produced in the joint resemble to a considerable extent those present in osteoarthritis. The course of the affection, however, is different. There are the same cartilaginous changes. There is a marked increase of synovial fluid, which bulges out the joint usually more than in osteoarthritis. There are also the same ridges of bone, or bony masses, formed around the articular cavity. The disorganization of the joint is apt to be rapid and pro-

nounced, with grating and creaking at times and a wide range of movement because of softening. Dislocation and fractures are apt to occur, with marked atrophy of the neighboring muscles.

At times the rapidity of the course is extremely rapid, complete disorganization occurring within a few weeks, even though the joint has been kept in a state of perfect rest.

The pathogenesis of Charcot's disease, from my viewpoint, is explainable when the fact is recalled that the nutrition of all osseous tissues and their related structures is due to the volume of arterial blood which they receive. This arterial supply being governed through the spinal system, lesions of the cord which impair or arrest the functions of the spinal nerve-paths inhibit more or less the nutrition of the tissues to which their terminals are distributed by reducing the volume of blood they receive to carry on their vital process. In Charcot's disease, the joint or joints become disorganized owing to diminution, below the required volume, of the arterial blood locally supplied.

TREATMENT.—At the present time virtually nothing is done for these cases but to protect the joint by means of **rest** and a **supporting apparatus** to relieve it of weight. Tapping and the injection of phenol have been advocated, but without apparent benefit.

Of late, however, more active measures have been recommended by surgeons, **resection** of the joint by some, for instance, and **amputation** by others. Most surgeons, however, oppose such radical procedures, even though Southam found in 4 instances that the stump, after amputation, healed without trouble

and, if the procedure was carried out under strict asepsis, without supuration.

These more radical procedures seem warranted from my viewpoint, because the joint lesions are essentially local, in the sense that it is only their arterial supply which is interfered with by the spinal lesions. Operative procedures elsewhere in the limb, therefore, need not be feared nor regarded as a source of danger.

The logical medical treatment, in the light of my views, is the use of vasodilators which, even though they may not improve or affect the spinal lesion, will materially increase the volume of blood, through collateral circulation, admitted to the joint. Such drugs as **arsenic** or the **arsenates**, **theobromine**, the **nitrites**, etc., by acting pharmacologically in this manner, might serve to counteract the local denutrition and thus save the joint. **Massage and re-education of the muscles** of the affected area should then be resorted to.

From experience in 10 cases the writer concludes that **fixation** and **arsphenamin** in Charcot's joint not only set a limit to the bone changes but lead to bone repair, the symptoms which persist being only those due to mechanical damage done before treatment. F. J. Cotton (Ann. of Surg., lxxii, 488, 1920).

TARSAL SCAPHOIDITIS.

SYNONYMS: *Freiberg's disease*; *Köhler's disease*.

SYMPTOMS.—This disorder of the second metatarsophalangeal joint was first described by Freiberg, and later, more comprehensively, by Köhler. It occurs in children and adolescents. Its manifestations are: Limping, pain, tenderness, swelling and redness over the inner dorsal surface of the foot.

X-ray examination shows definite and constant changes in the scaphoid bone, which is diminished in size, with an irregular, blurred outline.

Two cases added to the 48 found on record. The pain, limping, tenderness, and sometimes redness of the overlying skin are explained by the irregular outline of the unusually small, compact scaphoid bone in young boys. Girls are much less frequently affected. No complications have ever been observed, and conditions return to normal in days, weeks or months, as confirmed by roentgenoscopy 2 or 3 years later. Sonntag (Deut. Zeit. f. Chir., June, 1921).

The pathological changes consist of thickening of the distal end of the second metatarsal bone, with obliteration of the neck of the bone; shortening of its head; change in the distal surface of the joint; widening and irregularity of the space between the bones; calcifications in the joint capsule, and changes in the central part of the surfaces of the opposing first phalanx.

Chronic trauma is responsible for the affection. In 2 of the 24 cases on record it was bilateral; 15 of the patients were girls between 10 and 21. O. Schreuder (Deut. Zeit. f. Chir., Mar. 30, 1923).

TREATMENT.—This should be conservative. Immobilization in a **plaster-of-Paris cast** in severe cases, or **rest and adjusted shoes**, are alone indicated, as the disorder tends to correct itself as the child grows older.

The writer saw a 17-year old girl, a sturdy farm worker, accustomed to go bare-foot, showing all the signs of Köhler's disease. The thickening of the shaft of the second metatarsal is probably due to chronic irritation and functional adaptation. He recommends the ordering of **proper shoes** in such cases. **Extirpation of the joint** may be considered where the changes

are pronounced. Baensch (Deut. med. Woch., Mar. 10, 1922).

BERTOLOTTI'S SYNDROME.

This syndrome, as described by Armando Albanese (Chir. d. org. di movimento, Dec., 1921), is related to an abnormal development of the lateral processes of the fifth lumbar vertebra and to anomalous relations of this segment with the sacrum and the iliac bones. The resulting disturbances have been variously diagnosed as sciatica, persistent lumbago, coxitis, colic, appendicitis, spondylitis, etc.

The presence of the syndrome always implies *sacralization* of the fifth lumbar, but the presence of sacralization does not necessarily mean that there is also a Bertolotti's syndrome, as there may be no pain at all.

The syndrome appears generally in individuals between the ages of 25 and 30 years. The prognosis is usually favorable, though in some cases the pains tend to recur.

TREATMENT.—This consists of **rest** of the patient on his back, the use of **proper shoes** or, if needed, the application of **Volkman's extension apparatus** to the lower joints, and the use of **hypnotics**. **Galvanic and faradic currents**, **heat applications**, **vibratory massage**, and **radiotherapy** over the most painful points are also suggested. Where surgical intervention is necessary, **resection of the transverse processes** appears to be the best procedure.

TUBERCULOUS ARTHRITIS.

SYNONYMS.—*Gelatinous arthritis; scrofulous joint; strumous disease of the joints; tumor albus; white swelling.*

DEFINITION.—As its modern appellation implies, tuberculous arthritis refers to an inflammation of one or more joints due to penetration

therein of the tubercle bacillus. It may be localized, or occur in conjunction with tuberculous infection elsewhere in the body, or may precede it.

SYMPTOMS.—Joint tuberculosis occasionally runs an acute course, exhibiting all the signs of inflammation, *viz.*, heat, redness, swelling, pain, and disturbance of function. The pain is not severe, however, except on motion. When the epiphysis is involved the pain may be referred to some distant part, *e.g.*, the knee in tuberculosis of the hip-joint. An important symptom is localized tenderness, whereas in other forms of infective arthritis the tenderness is widespread.

Commonly, the disease begins insidiously. Disturbance of function is apt to be the first symptom, particularly if the hip or knee be affected. The skin ordinarily remains white (hence the old name, "white swelling"); the joint becomes swollen, owing to the swelling of the synovial membrane and increase of fluid. Pain begins gradually, and, while sometimes almost entirely absent, at others is felt only on use of the joint.

Redness may occur when pus has formed and is working its way toward the surface. This takes place usually at certain definite spots, which break down and form sinuses, leading down to carious bone and, in cases of long standing, directly into the joint. The pain is felt in the joint itself, in the epiphyseal ends of the bones, and, as we have seen, at times in remote parts. Fluctuation is seldom elicited as it is in a syphilitic joint, but there is, as a rule, reflex spasm of muscles, followed by muscular atrophy and subluxation of the joint.

In some cases, especially where the lesions are multiple, doubt may arise

as to whether the affection is syphilitic or tuberculous. In these the von Pirquet test is valuable in children, while the Wassermann reaction is of service in both children and adults.

In a child suffering from a tuberculous joint, the night symptoms are suggestive. The child is very restless while sleeping, tosses and moans, and is apt to have "night-terrors," *i.e.*, cries out suddenly as if terrified.

Almost any joint can become affected, but the most commonly attacked are the spine, hip, knee, ankle, elbow, and wrist. The small bones and joints of the foot and hand are also not seldom involved.

In early cases of suspected joint tuberculosis in which a positive diagnosis cannot be made by ordinary methods, the writer performs an exploratory operation. He condemns conservatism, awaiting developments, because once immobilization is started the condition is obscured indefinitely. Of 25 joints explored, 18 involved the knee, 4 the hip, 2 the tarsus and 1 the ankle; tuberculosis was found in 18 cases. Primary union followed in each instance. In the knee cases, a fairly long incision to the inner side of the patella was made for inspection of the joint and removal of small pieces of tissue for examination. The only reliable test proved to be guinea-pig inoculation; this is, however, inconclusive when negative. De F. Smith (Jour. Amer. Med. Assoc., Nov. 15, 1924).

The prognosis in tuberculous arthritis was formerly discouraging, although in cases that were identified early as tuberculous, recovery was obtained with more or less ankylosis, partial or complete. Even now, if a cure be obtained, the tuberculous process may develop elsewhere long after the supposed recovery, while the intervention of pus organisms may

cause septicemia. The latter complication, disseminated tuberculosis, intense secondary anemia, amyloid disease and exhaustion, are the chief causes of death. As shown under TREATMENT, however, the more recent contributions to our knowledge have greatly improved the prognosis.

PATHOLOGY.—Although the initial infection may occur in the structures about the joint, the synovial membrane or the joint capsule, it practically always takes place primarily in the bone—in nearly 99 per cent. of knee-joint cases, according to Murphy. This entails destruction of the cartilage and penetration of the joint and synovial membrane, with formation of sinuses. This is followed by the formation of granulation tissue in the synovial membrane, capsule and periarticular tissues, and finally, by caseation. Soon thereafter stiffness of the joint occurs, due mainly to the muscular spasm caused by the presence of the morbid process, *i.e.*, reflex rigidity. This, in turn, compromises nutrition of the muscles involved, gradually causing their atrophy.

In *children* chronic articular tuberculosis may present itself as a fungous osteo-arthritis, a serous arthritis accompanied by hydrarthrosis, or as polyarthritis of various types. The fungous affection attacks the larger joints; the second condition affects especially one or both of the knees, while polyarthritis may be deforming or ankylosing, or may be evidenced by a chronic polysynovitis. No articular deformity or bony changes occur in chronic polysynovitis, which may present initial acute or subacute exacerbations. In a case of this kind treated by the writer, in a child of 11, fever, emaciation and tracheobronchial adenopathy were present. Improvement was obtained with **heliotherapy** and **tincture of iodine** in doses ascending

from 85 to 150 drops daily. Nobécourt (*Méd. infant.*, Oct., 1924).

TREATMENT.—**Fresh air and sunlight**, with careful, persistent, protective and conservative treatment, constitute the keynote of success in the management of tuberculous joint diseases. This applies particularly to the tuberculous arthritis of children. Tuberculin does harm at every stage; the various sera tried by some observers likewise, when subjected to controlled trials. **Heliotherapy**, with **immobilization** of the joint and suitable injections of antitoxic preparations, summarizes the best course to adopt.

Heliotherapy, as practiced by Rollier, of Leysin, Switzerland, who gave the method its modern impetus and demonstrated its therapeutic value, is to expose the little patients to the sun progressively, at first only the feet for 5 minutes 3 times a day, then the leg, then the arms, and finally the back and abdomen on the seventh day. The skin becomes red or dark brown, and this pigmentation appears to be an important factor in the cure. Phagocytosis is increased. The **dry, cold air of high altitudes** is a valuable aid to the sunlight. Plaster casts are not used, **immobilization** being secured by linen hands or jackets that may be loosened for exposure to the sun. Joint function returns almost always, while tuberculous glands become softened and absorbed. Pain is arrested early in the treatment. Tuberculous abscesses are not opened in this treatment.

In this country excellent results are likewise obtained. At the J. N. Adams Memorial Hospital, the favorable progress, according to Hyde and de Grasse (*Amer. Jour. of Tuber.*, Apr., 1921),

is in direct proportion to the intensity of the pigmentation of the skin, which is used as an index to prognosis. The most striking local result, and the one of greatest importance and advantage in early cases, is the preservation of motion in the affected joint. The sun acts as an agent of repair on bone tissue. The effect on sinuses and ulcers is one of marked reaction. The effect on lymph-nodes is a gradual reduction of their size, and in broken-down nodes the contents are often absorbed. The effect on effusions in the joints and the peritoneal and pleural cavities is absorptive.

Living in a shack or tent is best. If the patient is treated in a ward or private house, the windows should be kept open day and night and closed only to exclude rain or snow. The temperature should not be allowed to exceed 60° F. (15.6° C.), even in winter, and the patient should be kept comfortable with woolen underclothing, jackets, and abundant bed covering. It is astonishing how quickly even children accustom themselves to the low temperature. The lesion or sinus, if any exist, is to be covered with a layer of gauze to protect it from flies, etc. On the whole, the value of **heliotherapy** has been amply demonstrated, and it should be carried out to the greatest possible extent.

As I have pointed out elsewhere (*Med. Jour. and Record*, Sept. 15, 1926), the manner in which these wonderful results are obtained is as follows: Briefly, the solar radiation, by liberating heat energy in the tissues, accomplishes what the reaction between the oxidizing product (adrenoxidase) of the adrenals, and the tissue lecithin, which is rich in phos-

phorus, itself brings about. Through enhanced activity of the cellular enzymes, including those of the phagocytes, their bactericidal and antitoxic power is greatly increased, along with all other cellular vital activities, including the processes of repair. Hence the curative efficiency of heliotherapy and, to a less degree, of other forms of treatment in which heat is the active agent.

Heliotherapy in the home can be effectively applied, according to A. O'Reilly (Jour. Mo. State Med. Assoc., Feb., 1924), but the technique is rather exacting and must be closely followed. The exposures are begun as soon as the weather permits in the early spring, and are given daily until the cold days of fall, except in bad weather. The several segments of the body are exposed in succession, the time being increased 5 minutes daily until all of the body except the head is treated and the total exposure reaches 2 to 3 hours twice a day. The exposures are given in the early morning and late afternoon. Overexposure is indicated by headache and fever. The head and eyes should be protected. Exposure through closed windows is inadvisable, the glass cutting off some of the violet rays. Sinuses are exposed last.

Open-air life is an essential adjunct, preferably in a well organized sanatorium, but if not, by the utilization of a protected porch or even rooms with open windows, but so disposed as to avoid draughts.

Immobilization and extension, if a limb is the seat of the lesion, are important features of the curative treatment. The main element required is **rest**. Tuberculous attacks often fol-

low injuries. Furthermore, the disease is kept active by repeated, slight irritations due to movements and use of the part. Therefore protection is required. The more acute and marked the trouble, the more absolute must the rest be. It is practically impossible to secure this when the spine, knee, or hip is affected unless the patient is placed in bed.

Parents, and even physicians sometimes, believe that prolonged **rest in bed** will be injurious to the general health, but experience has abundantly proved that this is not so, and whenever it is possible to do so the patient should be put abed and kept on his back until all symptoms of activity of the disease have subsided. This should be done for months or even a year or two if necessary.

To keep small children in bed and prevent their sitting up, it is desirable to fasten them down by means of a towel passed across the chest and pinned fast with safety pins to the mattress. **Bradford** devised a **frame** of iron gas-pipe to surround the child, covered with canvas or unbleached muslin. The child may be fastened to this by means of a sort of apron extending across the chest with straps passing over the shoulders. This is useful in affections of the hip as well as of the spine.

Extension is of service in diseases of the hip and knee; its object is to keep the joint-surfaces from being pressed together by muscular contraction. Its good effect is at once seen by the diminution of pain. It allays muscular spasm. Even when the patient is allowed to go about, the same object is aimed at by the use of a suitable apparatus.

All these measures are indicated

even in the presence of pus, unless persistently high temperature and severe pain prevail. Active intervention then becomes necessary. It should be remembered, however, that infection is very liable to attack a discharging collection of tuberculous pus, and the general health may become affected.

Abscesses may be emptied with a **trocar**, washed out with **salt solution** or a weak antiseptic, and then injected with 10 per cent. **iodoform emulsion**, 1 ounce (30 c.c.) or more being used. This will have to be repeated perhaps two or three times. It is especially useful when no bone disease is revealed by X-ray examination or incision.

Another valuable procedure in such cases is the Murphy 2 per cent. solution of **formalin in glycerin** (24 hours old), injected in 2 to 4 dram (8 to 16 c.c.) doses, according to the size of the joint treated, after **aspiration**. This tends to favor the formation of fibrous tissue, which encapsulates any tuberculous focus reached and promotes recovery. Where there is septic infection in addition to the tuberculous process, **scraping of the sinuses** followed by **plugging** with gauze soaked in a 5 per cent. **formalin** solution is very effective. It should be remembered that formalin is painful and that light anesthesia, *e.g.*, by **nitrous oxide-oxygen**, is necessary in most cases. The diseased area should not be allowed to bear weight for at least six months, and then only with due care and close watching.

In elbow and wrist cases **Bier's hyperemia** is often helpful, but not in the exudative form. The band should be broad (6 cm.), soft, applied slowly and evenly around the extrem-

ity, proximally, but not close, to the tuberculous joint. It must not cause pain. It is applied once or twice daily, for from one to two hours. Considerable time is required for a cure—nine months or even longer. The treatment is inapplicable to the hip-joint. It should be avoided when the lungs are seriously involved, or if there is marked amyloid degeneration. It has the advantage of permitting early passive and active motion even in severe cases.

Bismuth paste has yielded successful results in sinuses or fistulæ of tuberculous joint disease that have been discharging for one or more years; these can be cured within a couple of months.

As prepared by Beck, who introduced the method, the paste contains 30 parts of bismuth subnitrate and 60 parts of vaselin, well stirred while boiling, with 1 per cent. of formalin added. Large quantities of the paste may prove toxic; therefore it should be used only for small cavities. Any sequestrum or pus should first be removed, and the cavity next **washed out with saline solution**. The paste, sterilized, is then injected and left in. It distends the cavity and sinuses and affords a support for the growth of granulations. A thin gauze pad is then applied, and an ice-bag placed over it to harden the paste. Later, the vaselin paste is replaced by a harder one, prepared by the addition of 5 parts of paraffin and 5 of white wax. To avoid poisoning, Blanchard recommends the use of a **pure white wax paste in vaselin**, used in the same manner. Plain **vaselin** has also been employed.

With this treatment, again, patients are to be kept in bed until all evi-

dence of acute trouble has gone and this result has been maintained for two or three months. The patient may then be allowed to go about with some appliance to keep the joint from moving, or with a **high shoe and crutches**. These **protective appliances** are to be worn for months after all evidence of active disease has disappeared. For walking cases, satisfactory appliances that can be used for many months may be made of sodium silicate. An apparatus prepared by the instrument-maker is much to be preferred for all tuberculous cases.

While the local treatment by **rest**, *i.e.*, **immobilization**, etc., helps to subdue local symptoms, the curative process proper requires hygienic measures, particularly the **open-air** treatment and **heliotherapy**, previously described. These are at least as useful after the active treatment of the joints as before the need of it arose.

Resection of joints is to be resorted to when suppuration is so profuse as to endanger life and the patient is of a suitable age. Resections in young children interfere so much with growth as not to be advisable. In these patients, partial resections or **erasions** are to be preferred, the joint being opened and the affected tissue cut and gouged away. Operative measures become more advisable as the patient increases in age. **Amputation** is to be resorted to only as a life-saving measure, usually for profuse suppuration with entire disorganization of the joint.

An important point emphasized by Perthes in this connection is that a poor general condition or lung tuberculosis often improves with great rapidity after the diseased joint has

been disposed of. The social condition of the patient is also of import. In a laborer, experimentation with rest, iodoform injections, or Bier hyperemia will often be impracticable, whereas by joint **resection** he can be enabled to work in 2 or 3 months.

In the operative treatment of tuberculous joints the author uses **Kocher's incisions**. All tuberculous tissue should be carefully **excised** by exact dissection. If the bone is involved, the bone ends are exposed by energetic dislocation. **Iodoform powder** is always used, but previously prepared by boiling for $\frac{1}{2}$ hour in 1:500 **bichloride solution**. The powder is rubbed into the entire wound surface, bone and soft tissues. The superfluous, loose part of it is washed away with **saline solution**, thus avoiding dangerous degrees of iodoform intoxication. In all **resections** wound cavities are drained with rubber tube surrounded by washed out iodoform gauze strips. Plenty of absorbent gauze and cotton is used for dressing. A **plaster-of-Paris cast** is put on before the Esmarch bandage is released, and the drains removed through windows in the cast within a week. Later, a light **cast** is used. G. Schwyzer (Surg., Gyn. and Obst., June, 1920).

As urged by the late Gwilym G. Davis, **mechanical supports** or **splints** of some kind are of the greatest service. Plaster-of-Paris and sodium silicate are of great utility; likewise splints made of pasteboard, wood, or leather. When quick setting is required, or frequent changing, plaster-of-Paris is best. When the patient can remain in bed for twenty-four hours, and where quick setting is not required and the apparatus is to be worn for a considerable time, then sodium silicate is preferable. For the upper extremity splints of wood, pasteboard, or leather are applicable. These various dressings, however,

can be used in any part of the body, and the choice will depend on the peculiarities of the individual case and the mechanical abilities of the surgeon. The dressings should all be so made that they can be removed every day or two, in order that the parts may be inspected and bathed and excoriations prevented. In spinal disease, when the patient is not fastened down in bed, it is desirable that the apparatus be worn during the night as well as by day; this insures better rest to the diseased part.

Local applications no longer play an important part in the treatment, though in *acute cases* evaporating lotions such as **lead water** may be applied, or an **ice-cap** laid on the **inflamed joint**. When the disease becomes more chronic, then **ointments of, e.g., belladonna and mercury** and 10 per cent. **ichthyol** may prove useful, the joint being firmly bandaged with either a **flannel** or **rubber bandage**; or, it may be **strapped** with adhesive plaster.

The **X-rays** seem to be gaining favor, though their mode of action remains unexplained.

Cure obtained by **X-ray** therapy in 73 per cent. of 270 cases of enlarged glands; 14.8 per cent. more were improved. Excellent results have been published by others with **X-ray** treatment of the shoulder and elbow joints, but conditions are less favorable for it in the knee and ankle. Edling (Paris méd., Feb. 6, 1926).

PONCET'S TUBERCULOUS ARTHRITIS.

SYNONYM: *Tuberculous articular rheumatism.*

DEFINITION.—A form of arthritis produced by tubercle bacillus toxins in the arthrodial fluids, without the presence of bacilli themselves

or tubercles in the joint, and occurring in some instances as the initial manifestation of a tuberculous lesion at a point in the body other than the affected joint or joints.

SYMPTOMS.—The joint or joints involved may not be one or more of those which would ordinarily be thought of as likely to be the seat of arthritis, such as the knee, elbow, hip, etc., but others which would be more apt to be overlooked. Thus, as observed by Matas, spinal rigidity, scoliosis, spondylosis, genu valgum, coxa vara and painful flat-foot, and in the head, dry otitis media with ankylosis of the ossicles, and various other osteoarticular disorders of children, adolescents and young adults, may, in many instances, be traceable to some toxemia of tuberculous origin, or focus in which the tubercle bacillus is active—a fact often suggested by the presence of fever.

The earliest manifestation is, perhaps, pain in the joint—a simple arthralgia suggesting a mild attack of acute rheumatism. Attacks recede and reappear, however, the recurrences becoming gradually more serious and involving an increasing number of joints. The arthritis then assumes chronicity, some cases, however, eventually proceeding to recovery if the causal tuberculous focus itself becomes harmless through sclerotic or other natural protective resources, while others become progressively worse.

If the morbid process persists, the joint symptoms assume greater gravity, and the aspect of a general infection is added: Fever, with rapid pulse, sweating, and if the lungs are involved, the signs of a pulmonary infection, or of pleural involvement.

The pericardium, meninges and other structures enumerated above may individually or severally become the seat of a primary or secondary tuberculous infection.

The majority of cases, particularly under the influence of modern methods of treatment, proceed to recovery—some of these, however, permanently deformed or crippled. The remainder die as a result of the associated or causal tuberculous processes.

TREATMENT.—The therapeutic indications applying in tuberculous arthritis, described under the preceding heading, are applicable here. The essential feature is early diagnosis and treatment of the causal area of infection, in addition to the local lesions. The article on TUBERCULOSIS, in the eighth volume, will throw light in this direction.

SYPHILIS OF THE BONES AND JOINTS.

The general subject of SYPHILIS and its treatment is considered at length under that head in Volume VIII, to which the reader is referred.

The *bones* are frequently involved in syphilis where early and proper treatment of the disease has not prevented such involvement. The periosteum and underlying bone may at times become the seat of an inflammation of merely temporary duration. This osteoperiostitis may, however, and often does, assume more severe proportions. Pain, which is much worse at night—the “osteocopic” pains—is then a prominent feature of the case, the affected area of the bone becoming tender. The bones most frequently involved are the tibia, clavicles and skull, headache, due to periostitis of the inner table of the skull, often assuming a very severe character.

The areas of periostitis, wherever formed, tend to form a soft node, which eventually becomes a hard node through ossification. Lesions of the periosteum and bone usually appear with or soon after the onset of the secondary eruption, though in rare instances they precede it.

The *joints*, when involved in syphilitic infection, simulate articular rheumatism very closely, particularly during the secondary stage. The pain, however, as is the case with bone syphilis, is worse at night; the whole course is milder, the stiffness much less marked, and the endocardium not affected. The pain may, however, antedate the secondary eruption. Synovitis, both acute and chronic, is also observed, developing suddenly with tenderness, pain, swelling, and more or less fever.

Although sometimes termed “syphilitic rheumatism,” this condition is not attended by the sweating of acute rheumatism. It also lacks cardiac complications; there is no cutaneous redness over the joint, and it does not migrate. Hydrarthrosis may develop at any stage.

Syphilitic arthritis may occur in infancy, from heredity, in the secondary stage, or in the tertiary stage. In infancy, and also to a somewhat less extent in adults, the disease is to be recognized not so much by its own peculiarities as by its surroundings and associations. If there is any point that may be more noticeable in it than in other affections of the joints, it is its less acute and less painful course. In infancy the joint, particularly the knee, may become swelled and somewhat—but not exceedingly—painful, nor very red, but be held stiff, with accompanying atrophy of the muscles.

There are usually present other manifestations of the disease, such as skin eruptions, eye affections, notched or pegged teeth, etc. A syphilitic history may also often be traced in the parents. Syphilitic arthritis in infancy may assume mostly the synovial type.

During the third stage of syphilis the joint may become the seat of a deposit of gummatous tissue distributed unevenly in it. The swelling may then be more irregular than in rheumatic disease, the deposit occurring in some portions of the joint while other portions are free. As a rule, tertiary joint syphilis does not occasion suppuration, although ankylosis may occur. This ankylosis may be fibrous or even bony.

TREATMENT.—The general treatment of syphilis being considered under **syphilis** in Volume VIII, only those features which bear upon the joints themselves will be referred to here.

The effects of **mercury**, preferably the **biniodide**, on the hereditary form of syphilitic arthritis are promptly manifested. In adults mercury **biniodide**, $\frac{1}{16}$ to $\frac{1}{8}$ grain (0.004 to 0.01 Gm.), and **potassium iodide** in 5-grain (0.3 Gm.) doses, both agents being given thrice daily, will also act promptly. Where, as is often the case, osteochondritis is present, the pain ceases and healing occurs, after **opening of the joint** and **free removal of the necrotic tissues**, soon after administration of mercurials. After the reparative process has begun, **gentle massage**, **baking** and **counterirritation** with **iodine** are believed to hasten recovery.

C. E. DE M. SAJOUS,
Philadelphia.

JOINTS, SURGICAL DISEASES OF.

LOOSE BODIES IN JOINTS.

This condition is most common in adult males. In the vast majority of instances the knee is the joint affected. Aside from dislocation of the semilunar cartilages of the knee, discussed elsewhere (see **DISLOCATIONS**, Vol. IV), there are many cases in which partly or completely detached bodies of varying source give trouble in this joint. Such bodies range in number from one to hundreds, and in size, from that of a pea or less to that of a plum. The remaining joints in which difficulty from loose bodies may occur comprise chiefly the other large articulations of the extremities, especially the elbow, and occasionally the temporomaxillary joint.

SYMPTOMS.—In some instances loose bodies cause no symptoms, remaining ensconced in recesses of the joint. In other cases abrupt appearance of symptoms may occur as a result of pinching and jamming of a loose body while the joint is in motion. In other cases still, the loose body or bodies may by irritation induce a persistent synovitis, with some pain, slight swelling, and more or less disability of the articulation.

In those instances in which a loose body becomes jammed during articular motion, this fact becomes at once manifest—usually in walking, since the knee is the joint generally affected—in severe pain and locking of the joint in a certain position. Some patients are able so to manipulate the part as to free the jammed body, whereupon motion may be resumed. The loose body may itself soon slip out, even without manipulation, but in many instances it remains *in situ* for many hours or days. Unless its liberation is very prompt, acute synovitis and effusion into the joint follow the locking. Repeated attacks of this type are likely to maintain a state of chronic local irritation and arouse in the patient a sense of distrust in the function of the joint which leads to avoidance of its use. Even a very minute foreign body in a joint can produce trouble, according to Katzenstein, by causing reflex muscular contraction and thereby arresting the articular movements.

ETIOLOGY AND PATHOLOGY.—

In many instances loose bodies are the result of injury. The synovial fringes become inflamed, enlarged, then condensed, and finally often separated, leaving one or more bodies floating free in the joint. Such bodies are likely to contain cartilaginous tissue; in fact, according to Bland-Sutton, they result not only from enlargement, but also chondrification, of the villi of the synovial membrane. Sometimes the bodies are found still attached by a pedicle.

In König's experience, disturbance of the villi in the knee frequently appears a long time after injury. Sometimes the villi are congenitally large, and cause trouble from childhood on, greatly increased by injury. Occasionally folds and adhesions in the capsule are left after an injury and the villi are caught in the pockets thus formed. Where they cannot be felt from the outside, the diagnosis is probable if there is constant tenderness at one point in the capsule. Lefèvre and Dubourg regard the so-called "arborescent lipoma," villous polyarthritis, and Hoffa's disease (fatty synovial fringes, springing from the ligamenta alaria and mucosa and undergoing inflammatory hyperplasia) as being merely three forms of a single disorder which they designate as chronic fibroadipose synovitis.

According to Davis, some loose bodies in joints are mere masses of fibrin showing little or no structure.

In the case of the semilunar cartilages of the knee, which are particularly liable to injury, a piece of bone may at times be detached along with the cartilage. Aside from this, loose bodies at times contain calcareous or true bony material. According to König, loose bodies sometimes result from the tearing off of small pieces of bone by the crucial ligaments, and in other instances from necrosis following embolism of an artery in the articular surface. Large and dense loose bodies may be discernible with the X-ray, and in some instances a corresponding defect at the point from which the body became detached may be detected.

Apart from injury, loose bodies are frequent and at times very numerous in osteoarthritis (arthritis deformans). Super-added trauma would, of course, promote detachment of the hypertrophic masses.

TREATMENT.—Where a loose body has given rise to locking of the joint, **forced flexion** followed by **sudden extension** may bring relief. If the internal semilunar cartilage is responsible, a useful maneuver, according to Lane, is to separate forcibly the internal condyle of the femur and the tibia by flexing the knee and at the same time abducting it, using the external condylar joint as a fulcrum.

While, in general, loose bodies are curable only by operation, the treatment of "caught fringes" in the knee may be conservative if they are causing only moderate disturbance (Rammstedt). Gradual return to normal generally follows **massage**, heat in the form of **sand bags** or **hot air**, **elastic compression** by bandages, and guarded use of the joint with apparatus. Upon prolonged immobilization with **splints** or **apparatus** loosened parts may become fixed or cease to give trouble. Where trouble occurs only after twists of the knee, the **Shaffer brace**, which allows flexion but prevents rotation, frequently gives complete relief. Other forms of apparatus provide means to check excessive flexion, where this is observed to cause difficulty. In persons who refuse an indicated operation, a simple **elastic knee-cap** may be of some help.

Surgeons generally advise prompt **operative removal** of loose bodies in order to cut short joint irritation and remove the probability of later impairment of joint function, besides relieving the immediate symptoms. This applies particularly to loose bodies traceable to injury, but according to Kappis, where arthritis deformans exists (in the elbow and knee especially) and is not too far advanced, actual recovery from this disorder often follows the mere removal of loose bodies.

Davis found the following procedure most satisfactory: The surgeon feels for the loose body, and when it is found crowds it into some corner and holds it there persistently with his thumb. The patient is etherized and an incision made with the other hand down to the joint capsule directly over the loose body. A pin is then thrust into the latter and an incision made directly through the capsule and the loose body turned out. The capsule need not be sutured, two or three deep

interrupted sutures to close the wound sufficing. The favorite places for loose bodies in the knee, according to this observer, are on each side of the patella (low down in the case of the inner side).

Many other surgeons operate under local anesthesia. The loose body may be fixed with a pin before the operation is started. The joint, when opened, may be explored, with the finger to detect any other loose bodies. Pedunculated bodies are removed by severing their pedicles with scissors. If hypertrophic "fringes" are responsible for the symptoms, they are seized with forceps and likewise excised with scissors. Unusual care as to asepsis is imperative. The opening made may be closed in two or three layers, *e.g.*, synovial membrane, capsule, and skin.

Willems advocates **active movements** beginning as soon as the patient awakens from anesthesia, with **walking**, unsupported, on the second or even the first day.

For "joint mice" or foreign bodies in the posterior portion of the knee-joint, Brackett and Osgood have used successfully a 10-cm. (4-inch) incision in the popliteal space, slightly within the median line, with removal of the loose body by opening through the posterior ligament and capsule.

Anteriorly, for wide exposure, **transverse** or **longitudinal** (Jones) **section of the patella** has been availed of.

In a case of loose cartilage in the temporomaxillary joint, with inability to close the mouth, Behan operated with satisfactory results.

ANKYLOSIS.

This term refers to stiffness or rigidity of a joint.

Ankylosis is qualified as *complete* or *bony* where the adjacent bones have become united by osseous tissue, and as *incomplete* or *fibrous* where the restriction of motion is due to fibrous bands. A further division is made into *true* or *intra-articular* ankylosis, in which the joint surfaces are united by fibrous tissue, cartilage or bone, and *false* or *extra-articular* ankylosis, in which the rigidity is due to structures outside of the joint, *e.g.*, fibrous cicatrices, contracted muscles or fasciæ, or adhesion of tendons.

ETIOLOGY AND PATHOLOGY.—True ankylosis results from synovitis or

arthritis of varying causation, *e.g.*, infection by pyogenic germs, the gonococcus, the tubercle bacillus, or the treponema of syphilis. All joint inflammations, if sufficiently severe and persistent, are liable to induce ankylosis. Joint suppuration does not, however, necessarily end in loss of joint motion. Bony ankylosis is preceded by fibrous ankylosis, during which the joint generally undergoes increasing flexion until the time when union is complete.

Ankylosis may also result from fracture near to or involving the joint, from unreduced dislocation, from caries which so alters the shape of the bones that normal motion is not possible, and from osteitis deformans. Prolonged immobilization of uninfamed joints does not lead to ankylosis, although there may be some stiffness because of atrophy of the structures surrounding the joint.

False ankylosis results from various forms of paralysis attended by muscular contracture and from injuries leading to extra-articular fibrous change and adhesion.

DIAGNOSIS.—The recognition of intra-articular ankylosis calls for a preliminary inquiry into the condition of the muscles, to exclude these as the source of the rigidity. Abnormal contraction of the muscles is readily detected by palpation, and is often only temporary. Absence of pain on attempted passive motion points to bony ankylosis, as does also absence of voluntary motor power, the result of muscular atrophy succeeding such ankylosis.

In doubtful cases considerable information is obtainable by examination under anesthesia, which eliminates pain and muscular action. Such examination may be prejudicial, however, if arthritis, including the tuberculous variety, is present. Aside from such cases, the examination under anesthesia will often reveal the existence and extent of bony union, whether the ankylosis is merely fibrous, and whether fibrosis is within or outside of the joint.

X-ray study, especially with stereoscopic views, is of assistance in revealing the exact reciprocal relations of the bones, the extent and situation of the ankylosis, and the nature of the material causing rigidity.

TREATMENT.—The prophylactic treatment of ankylosis comprises the application of such measures as are indicated

in the individual type of case to restrict effusion and inflammatory exudation into the affected joint, together with early **passive movements** to hinder intra-articular adhesion. Such movements should not, however, be pushed to the point of causing severe, long-continued pain, the latter suggesting that more harm than good may have been produced. Particular caution should be exercised in tuberculous cases, in which a premature attempt to restore motion is apt to relight the trouble.

In acute joint infections, to prevent ankylosis, J. B. Murphy advocated **extension** and, where tension in the joint exists, **aspiration** followed by injection of 2 per cent. **formalin in glycerin**.

In established, but not dense, fibrous ankylosis the result of synovial adhesions, daily attempts at **mobilization**, with avoidance of violent pain, may restore joint motion more or less completely. Where such manipulation fails, resort may be had to the forcible breaking of adhesions under anesthesia (**brisement forcé**). The joint is alternately flexed and extended until as much motion as possible has been secured, generally under primary ether anesthesia, nitrous oxide or ethyl chloride. It should be remembered that excessive force may fracture atrophied bones or rupture blood vessels, nerves or other soft tissues, besides causing so severe an inflammatory reaction that adhesions will reform.

Generally, more is to be gained by not attempting too much mobilization at one sitting. After each manipulation, care should be taken to maintain the mobility gained; this is done by passive and active movements, instituted as soon as the inflammatory reaction induced has subsided under **rest** and **ice-bags**. Sometimes nothing more can be gained by manipulations than the placing of the limb in a more useful position. Where increased extension of a joint is particularly desired, application of some sort of a **splint** or **apparatus** that will hold the part in its most extended position, such device being removed daily for **passive movements**, is likely to be useful. Apparatus producing gradual pressure, such as the **Strohmeyer screw**, and the application of strong **rubber bands**, for either flexion or extension, have also been employed.

Brisement forcé is contraindicated in tuberculous arthritis.

In some cases no results whatever are obtained by manipulations; or, the condition may become worse than before. Radical measures will then alone avail.

Operation in bony ankylosis is undertaken either with a view to bettering the position of the part or for the purpose of forming a false joint (pseudo-arthritis). In this connection it should be kept in mind that in the lower extremity stability is of even greater value than mobility, while in the upper limb mobility is the more important. The operative indications also vary according to the relative need of mobility of the member in the patient's gainful occupation, whether infection is absent or has subsided or might be relighted by intervention, and whether toxic muscular atrophy has occurred.

Osteotomy, in which the bone is broken after it has been partly cut through with the osteotome and is then immobilized for consolidation in the improved position, has been employed particularly for ankylosis of the knee and hip. In the case of the knee the femur is divided above the joint; the position of extension is usually the one sought. In ankylosis of the hip in a bad position, an incision is made vertically downward from the vicinity of the anterior superior spine and the osteotomy carried out either through the neck of the femur or as a **subtrochanteric osteotomy**. By securing a position of slight flexion and abduction, with a few degrees of outward rotation, a gait approximating the normal may be afforded the patient.

In the case of the elbow, good results are obtained by **resection (excision)** of the joint, which frequently yields serviceable mobility. As healing progresses, the joint becomes a useful one. The same operation is feasible in shoulder ankylosis, although with this joint, ankylosis is less disabling than in other joints, and in many instances operation is deemed unnecessary.

In the operation known as **erosion** or **arthrectomy**, the disease tissues alone—generally tuberculous—are removed. This procedure, where feasible, has the advantage over resection of causing no shortening and of avoiding, in children, subsequent deficiency of growth of the limbs.

An ankylosis of the temporomandibular joint is usually treated by **resection**, which has sometimes been carried out from within the mouth. R. T. Morris, however, as a preliminary step, has simply divided the bone with a sharp chisel below the point of ankylosis, and has found that this sometimes gives a mobile fibrous joint.

Stiff metacarpophalangeal joints, according to Dickson, can be gradually flexed by means of plaster. With a retaining **splint** the **flexion** is then maintained between **massage** treatments until there is full voluntary flexion and no tendency to relapse. Heyman similarly advocates prolonged massage and **manipulations**, or constant traction and flexion with Danforth's **banjo splint**. In refractory ankylosed fingers in manual workers, in whom a stiff finger is much in the way and subject to injury, **amputation** may prove advisable.

Modern surgical advancements in relation to ankylosis have centered mainly about **arthroplasty**, *i.e.*, an operation planned to reconstruct in some degree the component parts of a normal joint. The chief feature of the operation has usually been the interposition of some foreign material or soft tissue between the bone ends in order to prevent re-ankylosis and facilitate smooth motion. Such materials as celluloid, rubber, chronicized pig's bladder membrane and Cargile membrane have nearly always failed to be of lasting value, but somewhat better results are obtained with flaps of fat, fascia or muscle. Murphy had considerable success with the insertion of fatty and fascial flaps in the elbow-joint, but was less successful with the hip, shoulder, and knee. He found that in successful cases a new "synovialoid" membrane, with lining cells identical with those in hygromas, and containing fluid resembling synovial fluid, was produced.

More lately free **fascia lata** has been by far the most commonly employed tissue for interposition. According to W. C. Campbell, however, arthroplasty is rarely permissible except when the ankylosis has resulted from trauma or acute infectious arthritis. The joints responding the more favorably are, in order, the elbow, jaw, knee and hip. In the knee, one large condyle and one shallow concave tuberosity will yield a satisfactory hinge joint.

Among 14 elbow arthroplasties, Campbell had but 3 failures. Good results may be expected, according to his experience, in 60 per cent. of well-selected hip cases and in 75 per cent. of knee cases. In knee cases with weak muscle power, atrophic changes and flattening of the articular surface after operation can be avoided by intensive **muscular training**, **physiotherapy**, and gradual increase in weight-bearing by the aid of the Thomas **caliper splint**. In tuberculous cases, according to Groves, arthroplasty is permissible only where the synovial surface is alone involved and the bones are healthy and firm.

Putti has interposed fascia lata with success in a large series of cases. Both epiphyses are covered with a free flap, fastened in place with a few catgut sutures. No drainage is used. **Traction**, with the limb in a **plaster splint**, is kept up for a month. **Passive movements** are begun on the tenth day by the patient himself, with simple apparatus fastened to the bed. As soon as the wound has healed, **hot air** treatment is begun, and it is kept up for several months. **Electricity** is held to stimulate the principal muscles better than massage. Mechanical treatment need not be begun till the twentieth day, and weight bearing is not allowed before the thirtieth day. The chances of success were found by Putti greatest with the elbow, and next with the knee, the jaw, and the hip.

Transplantation of joints has been successfully carried out, mainly by Lexer and Tuffier. Tuffier restored two ankylosed elbow joints with portions of joints from amputated limbs. Lexer has had no permanent success with transplantation of an entire joint, but has had almost uniform success with half-joint transplantations, in which, *e.g.*, in the case of the knee the upper end and articulating surfaces of the tibia are replaced. He found it unnecessary to retain the capsule on the transplant if the original capsule remains and can be fastened outside of the joint surfaces. In spite of the successes thus obtained, Lexer considers that the modern tissue interposition operations more nearly approach the goal in ankyloses, being more permanent as to results and not being dependent on homoplastic material, which is difficult to maintain.

JOINTS, SURGICAL DISEASES OF (*Continued*).

HIP-JOINT DISEASE.

DEFINITION.—What is usually known as “hip-joint disease” is tuberculosis of the hip-joint; but tuberculosis by no means includes all the diseases which may affect the hip. The hip may be affected by tuberculosis, by syphilis, by rheumatism, and by a variety of acute infectious processes subsequent to the occurrence of some acute infectious disease in other parts of the body, or may be the seat of a simple synovitis caused solely by trauma. A synovitis of the hip is usually associated with osteitis, but a synovitis may exist independent of osteitis and subside without the occurrence of any involvement of the bones.

The hip-joint is also the seat of arthritis deformans and Charcot’s disease, though the latter is rare, and occasionally loose bodies are found in it. Malignant tumors also may affect the hip.

Functional affections of the joint are usually traumatic neuroses, but may be considered here.

SYMPTOMS.—The symptoms of *inflammation* in the hip vary somewhat, according to the character of the inflammation present. If the hip is the seat of an acute synovitis, pain will be felt in the hip itself, which will be intensified by movement of the joint or by pressure over the neck of the femur at a point between the great trochanter and the crest of the ilium.

According to von Friedländer, when the hip exhibits a sudden and painful flexion contracture with abduction or slight adduction; when the joint is slightly swollen and tender, its mobility somewhat impaired,

while the glands are not affected and there is no muscular atrophy, the possibility of a benign, ephemeral coxitis should be taken into account.

Broca has urged the need of bearing in mind in the diagnosis the possibility of hysterical coxalgia.

Among the earliest symptoms of tuberculous hip-joint disease noted in the Mayo Clinic were muscle-spasms, limping, pain and atrophy. Pain is often referred to the knee-joint. Night cries are not in themselves diagnostic. H. W. Meyerding (*Minn. Med.*, Aug., 1918).

Stress laid on the apparently normal intervals between the periods of limping; pain in the knee without local findings, and pain in dorsal hyperextension of the thigh. The parents should be urged to bring the child back if the limping recurs. Magg (*Münch. med. Woch.*, Dec. 18, 1925).

The position of the limb is very characteristic. The thigh is flexed upon the abdomen, abducted, the toes everted, and the entire limb rotated outward. This position allows the capsule to contain the largest amount of fluid, and, in consequence, is the position of ease which the joint naturally assumes when overdistended. In cases of this sort, also, there is usually a distinct history of a traumatism immediately preceding the occurrence of pain. These cases are also extremely sensitive to any sort of motion. In standing, the patient bears all the weight of the body upon the sound side, and in consequence of the position of the affected thigh the gluteofemoral crease on this side is much less distinctly marked than on the well buttock. In cases where the joint is the seat of an acute infection following measles, scarlet fever, or the like, the same train of symptoms will be present, though the progress of the disease will be much more

rapid, while combined with the local symptoms will be found those of general systemic infection, and under these circumstances disintegration of the joint may progress with remarkable activity.

In **syphilis** of the hip, on the contrary, the disease may have been present for months without the occurrence of pain sufficient to attract the parents' attention. It is only when a marked limp becomes noticeable that medical advice is sought, and in some of these cases, when marked deformity is present and joint-spasm is very pronounced, manipulation seems to give rise to but trifling inconvenience, and the parents at times are loath to believe that serious trouble exists, in view of the fact that the child complains so very little.

Legg-Calvé-Perthes's Disease.—This appellation, as well as the terms **juvenile osteochondritis deformans of the hip**, **pseudocoxalgia**, and **coxa plana**, have been applied to a disease met with in children in the first decade of life, more common in boys (4 to 1), and the onset of which can often be associated with some injury. As described by H. Platt, during the phase of active symptoms such a case resembles one of joint synovitis which seems gradually to clear up, the diagnosis being made only by the X-ray. The *first stage* shows a mild limp, slight pain in half the cases, slight fever in a few instances, and varying degrees of muscular spasm. The *second stage* shows an intermittent limp, often inconspicuous spasm, the leg held flexed and adducted, limitation of hip movement, especially in abduction and internal rotation, an undue prominence of the great trochanter (without being raised above Nélaton's line), and slight muscular atrophy. The *third stage*, that of recovery, to which all cases attain, shows an absence of most subjective and objective symptoms but a persistence of trochanteric thickening and reduced range of abduction.

The X-rays show at first simple flattening of the head in the vertical diameter; later, more flattening with fragmentation of the bony nucleus of the epiphysis into several pieces so that it appears as if the femoral head were creeping out of the acetabulum toward the great trochanter, and still later, during the healing stage, a fusion of these fragments but persistence of the flattening. The angle of the neck with the shaft is perhaps normal, *i.e.*, there is no true coxa vara. The acetabulum also shows destructive changes, often becoming shallow.

Bilateral involvement is quite rare. There is some evidence of heredity. Rickets is most likely a chance association. The presence of a syphilitic infection in some cases seems probable.

The *treatment* consists in **immobilization**, to relieve the joint of weight-bearing, but this does not seem to influence the train of morbid changes. Operative intervention has no place in the treatment.

The Legg-Calvé-Perthes disease occurs between the ages of 4 and 12 years, and causes a limp due to restriction of of abduction and internal rotation. Legg's theory ascribes the changes in the epiphysis to secondary circulatory changes. The theory that they are due to bacterial infection has little support, since in 4 out of every 5 cases on record the cultures were negative. According to Jansen, the changes in the epiphysis and neck are secondary and adaptive changes to deformity of the socket. The prognosis is good. In the acute stage the leg should be **immobilized in abduction**. A **walking caliper** should be used for one year. H. F. MacAuley (Irish Jour. of Med. Sci., Dec., 1925).

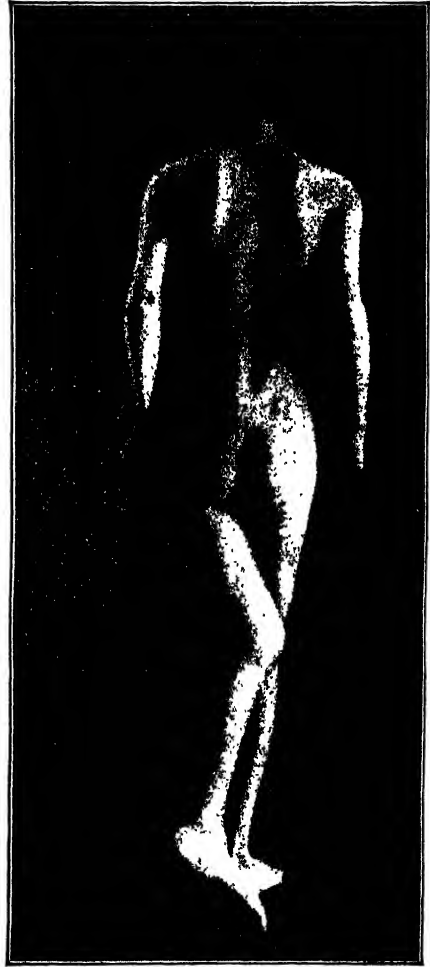
In tuberculosis of the hip the pain at the outset is not apt to be marked; but, should an abscess form in the femur or the disease progress until the cartilage becomes involved, the pain becomes most exquisite, children often crying severely from the jar occasioned by a person walking on the floor, and so shaking the bed.

In some of these cases there is a distinct history of traumatism, and in others it seems impossible to find precisely when the disease began, many of the cases which come to the surgeon with the history that the first symptoms were noted by the parents a few days previous being evidently of very long standing, the inattention of the parents to the trifling limp which the child exhibits, and the fact that it did not at first complain of pain sufficiently to attract their attention, being responsible for this. Quite frequently these children complain of being stiff on rising in the morning, and exhibit a decided limp, but after having been at play for some hours they run in almost a natural manner, and little is thought of it. In some cases this limp gets better and may almost disappear for a number of weeks, occasionally a couple of months, then reappear in a still more aggravated form, to subside once more, and again reappear. It is unusual, however, for cases to pursue this course, and the majority grow progressively worse, and do not, unless treated, exhibit these periods of freedom from symptoms.

The obturator nerve sends a little filament to the inner side of the knee-joint as well as to the hip-joint, and to this fact is due the characteristic pain in the knee which usually accompanies disease in the hip-joint, and which, in the great majority of cases, antedates the occurrence of pain in the joint itself.

Furthermore, the obturator nerve often joins the long saphenous, which accounts for the fact that pain in the big toe is very frequently noted before pain in the knee, which, however, seems to have escaped the at-

tention of a good many writers on this subject. Quite frequently children will be brought for observation because they limp and because they have complained of pain in the big



Fibrous ankylosis of the left hip-joint following typhoid fever, relieved by *brisement forcé*.

toe, which the mother had supposed was due to some defect of the shoe or stocking or an ingrowing nail. Examination in these cases will frequently reveal the presence of hip-joint disease.

One of the first signs which are present in inflammation of any joint

is spasm of the muscles controlling the motions of that joint. In hip disease efforts have been made to draw inferences, on account of the preponderance of spasm in a particular group of muscles, as to the location of the disease in the joint, but so far without having put us in a position to diagnosticate with exactness the location of the focus of inflammation from the presence of spasm in certain groups of muscles. Not infrequently there may be noted, in addition to the spasm of the muscles immediately controlling the joint, spasm of the calf-muscles, although attention has very seldom been drawn to this fact. It often will be seen quite pronounced in the early stages of the disease, when deformity is very slight and limitation of movement in the hip-joint but slightly marked. It will usually be found in those cases where pain in the great toe has been noted instead of pain in the knee.

Hand in hand with muscular spasm comes atrophy of the muscles affected by the spasm, and this atrophy shows itself too promptly to be attributed wholly to disuse, and seems to be dependent on impaired nutrition. It is one of the earliest and most important signs in connection with joint spasm in the diagnosis of incipient and doubtful cases, being of vastly more importance than the occurrence of pain; but usually it is not present until the disease has been in existence for some time.

The position assumed by patients with disease in the hip-joint varies according to the progress which the disease has made. At the outset the almost invariable rule is that the patient bears the weight of the body upon the sound leg, the toes of the

affected side being turned slightly outward, the thigh being flexed, the leg everted and slightly abducted; the buttock on this side is decidedly flattened, and the gluteofemoral crease lower down and more or less obliterated. On account of the abduction of the leg it seems longer than its fellow, but if accurate measurements be taken, with the limbs in the same relative position to the median line, this will be found to be an apparent, and not an actual, lengthening. As the disease advances, this distortion becomes more and more marked, until the thigh may be flexed almost to the point of striking the chest, and the leg everted and abducted to the limit of possible motion. If the capsule has been greatly distended with fluid, it may spontaneously rupture, or some sudden movement may rupture it, and the leg may pass in a very short time from the position of extreme abduction and external rotation to one of adduction and internal rotation. Quite frequently this change accompanying the rupture of the capsule is followed by marked relief from the pain of which the patient had previously complained. This position of adduction was formerly spoken of as the "third stage" of hip-joint disease, that of marked flexion and eversion being called the "second stage," while the former position of slight flexion was denominated the "first stage" of the disease. And for purposes of explanation, it possibly may be well to retain these terms in some cases, though they do not represent invariably the different stages in the progress of the disease, as we sometimes find cases with marked adduction in the commencement of the disease, though in such

cases we usually find the leg is rotated outward instead of being rotated inward, as it is when the thigh passes from the position of extreme eversion and abduction to that of adduction.

Coincident with the change of position from abduction to adduction, there comes a change from apparent lengthening to apparent shortening of the limb. If the disease has been in existence some time, there may be actual diminution in the length of the leg from absorption of bone, as well as the apparent shortening due to the adducted position in which the limb is held.

In *coxa vara* the lower extremity deviates toward the midline; this may be due to downward slipping of the head of the femur, deformity of the head or acetabulum, bending of the neck, or outward bowing of the upper portion of the femoral shaft, rachitic or traumatic. In *coxa plana* the diagnosis is usually made from the roentgenogram, which shows flattening of the head of the femur with irregularity of the border. *Arthritis* in children includes the infectious and suppurative type, the hypertrophic and atrophic deforming type, and Still's disease. The chronic progressive deforming arthritis is evidenced by atrophy of muscle and bones, contracture and eventually ankylosis. It may cease spontaneously at any stage. *Still's disease* is essentially the same, with the addition of enlargement of the lymph-glands and spleen. J. A. Key (Jour. Mo. State Med. Assoc., Nov., 1925).

DIAGNOSIS.—The diagnosis in hip-joint disease should only be difficult in the early stages. If a child is brought complaining of a limp, an obscure pain in the toe, calf, or knee, do not be satisfied with finding something in the toe, calf, or knee which may account for its limp and pain,

because it may possibly have disease of the hip in addition to its other ailments; but strip it, and watch its position with great care, allowing it sufficient time to become composed and assume its natural attitude, as quite frequently, under the influence



Appearance at the outset. (Sayre.)

of excitement, slight disturbances of function may easily be masked. After noting any of the abnormalities of attitude which have been just described, place the child upon its back upon a hard surface,—a table covered with a shawl, for instance. It is important that the surface be not so thickly covered as to leave a yielding

surface for the back to rest upon, as slight alterations in the position of the pelvis may then pass unobserved. With the normal child lying on its back, with its pelvis in such a position that a line drawn from the center of the sternum over the umbilicus through the symphysis pubis is at right angles to a line joining the two

leg gently to the table, and if there is involvement of the hip the psoas and iliacus or rectus femoris muscles will be sufficiently contracted to tilt the pelvis before the leg comes into contact with the table, and a slight arching of the lumbar spine will result. This tilting of the pelvis does not necessarily mean the presence of



Right hip-joint disease showing position in which leg must be placed to make back lie flat on table.

anterosuperior spines of the ilia, the entire back should rest upon the table while the lower extremities are in a straight line with the trunk, and also rest upon the table. If there is any arching of the lumbar spine, raise both legs until the entire spine rests upon the table, and then lower the side which you believe to be the sound one until the back of the leg rests upon the table. If the joint of that side be unaffected, there will be no change in the position of the trunk and pelvis, and the spine will remain in contact with the table. Now lower the other

hip-joint disease. It means a contraction of the iliopsoas muscle, which may be caused by inflammation of the spine, by appendicitis, or by salpingitis; but the previous history of the last two affections would exclude them from consideration, while careful examination of the spine should clear up the diagnosis between disease of the hip and disease of the spine, though in some cases both exist simultaneously, and the mistake of recognizing only one is sometimes made even by men of experience.

Both legs, lying flat upon the table,

should then be moved to and fro, to ascertain, if possible, the presence or absence of muscular spasm.

It is frequently advised that an anesthetic be administered, in order that the condition of a diseased joint may be thoroughly investigated. As far as diagnosis is concerned, this is absolutely unnecessary. The administration of the anesthetic, by the removal of the sensitiveness from the joint, removes the necessity which

nosis, is, first, to thoroughly gain control of the patient, and cause it to allow complete muscular relaxation, as a child will, in many instances, voluntarily stiffen its muscles when first examined, and thus mask the presence of a slight involuntary spasm. The joints should then be moved through all normal ranges of motion, beginning with the sound side, and slight involuntary twitches taken into account. It is usually



Right hip-joint disease, showing tilting of pelvis.

nature feels for establishing the involuntary muscular protection which she gives all inflamed joints, and thus removes from the surgeon a most valuable means of diagnosis. If the rigidity of the joint is due to adhesions, and so persists after the anesthetic has been administered, the case has been of such long standing that there should be no difficulty in reaching a diagnosis even by an inexperienced observer.

The mode in which to determine muscular spasm in the early stages of the disease, at which time it is most important to arrive at a correct diag-

quite unnecessary to manipulate the joint so violently as to cause pain, in order to arrive at a correct diagnosis, and, in the majority of cases, pain will not be elicited unless very extensive movements are made, and unless the limitation of motion which nature puts to the joint is violently overcome. Pressure over the hip-joint proper may at times give rise to pain; it very frequently does, but in many cases pain cannot be so elicited.

The length of the two lower extremities should now be noted, the distance from the anterior spine of the ilium to the internal malleolus

being taken as the most reliable measure; and in this connection care must be exercised that both extremities occupy the same relative position to the trunk at the time the measures are taken or they will be of no value, flexion and adduction causing much apparent shortening, while abduction causes apparent lengthening.

The relation of the trochanters to Nélaton's line should be noted, by passing a string from the antero-superior spine of the ilium to the tuberosity of the ischium. Normally this line should just touch the upper border of the great trochanter. If the latter lies above it, the cause may be fracture of the neck of the femur, congenital dislocation of the hip on the dorsum of the ilium, bending of the neck of the femur, absorption of the head or neck of the femur, or absorption of the upper part of the rim of the acetabulum, allowing the femur to glide upward. Which cause is present in each case must be determined by the surgeon.

Atrophy of the muscles occurs early in joint disease, and the circumference of each thigh should be noted, both at the upper portion and also at a point lower down,—say, 4 inches above the knee,—care being taken to measure the thighs at corresponding points, or the results will be useless.

In noting muscular spasm care must be had not to mistake the flaccidity of a paralyzed muscle for the normal state, and suppose the healthy side to be the seat of muscular spasm by contrast. The fact that the more relaxed thigh was the smaller ought to clear up any possibility of error, and it would seem that it hardly required mention save for the fact that such mistakes have occurred.

The temperature and pulse should also be noted, any elevation of the former above normal being taken, in a doubtful case of every incipient disease, as conclusive proof that disease is present, especially if there is present in addition an accelerated pulse.

The amount of elevation of temperature is a fair index of the violence of the inflammatory process.

Disease in the sacroiliac joint should be differentiated from hip-joint disease primarily by the position which the patient assumes while standing, the body being sharply bent through the lumbar spine, away from the diseased side, in order to free the articulation from pressure. This position, which is typical of disease in the sacroiliac or sacrolumbar joint, is not easy to describe, but, once seen, cannot be mistaken for anything else. Pressure of the two ilia toward each other gives rise to pain by compression of the diseased joint. Pain, in like manner, would be produced if pressure were made with the hands on the great trochanters, which might lead to doubt as to whether the disease were in the sacroiliac or the hip-joint; but if the disease were in the hip-joint and the pain were caused by pressure with the hands on both trochanters, pain would not be caused by pressing the ilia together with the hands behind the hip-joint, and the diagnosis would be cleared up in this manner. Direct pressure over the sacroiliac joint also gives rise to pain, and rotation of the hip fails to produce muscular spasm.

Congenital dislocation of the hip may be mistaken for hip-joint disease, but the history is different: there is no history of traumatism, and there is usually no history of pain. The dis-

turbance of gait has been noticed from the first efforts at walking, which generally have been made long after the time at which children ordinarily commence to walk, and there is usually marked prominence of the buttock on the side of the dislocation, and while the child is recumbent the head of the bone can be caused to glide upon the dorsum of the ilium, while the great trochanter is felt to approach and recede from the crest of the ilium. The only point in common with hip-joint disease is the limp, which, however, is different in its characteristics from the limp of hip disease, and the fact that the great trochanter is above Nélaton's line. In hip disease the trochanter would only be above Nélaton's line in an advanced case, whose history would be absolutely different from that of congenital dislocation of the hip.

Confusion may arise at times in regard to **fractures of the neck of the femur** in small children where there is a history of traumatism, pain, and limping, but the diagnosis can usually be made by the fact that the disability and the pain immediately followed the traumatism, and the great trochanter was immediately found to be above Nélaton's line; the only confusion possible being in cases which do not come under observation for months after the occurrence of the symptoms and where no history can be obtained. Such cases often present a picture of flexion and adduction which greatly resembles that of old hip-joint disease with absorption of the head of the femur.

In **coxa vara**, caused by the bending of the neck of the femur, the diagnosis is more obscure. In these cases, also, the great trochanter may be

above Nélaton's line. The motion of the joint may be limited, but careful investigation of the relation existing between the trochanter and the head of the femur, in combination with the direction of the neck of the femur to the shaft, and differentiation between the limitation of motion produced by spasm of the muscles and that caused by abnormal relations of the neck of the femur, which cause the latter to strike the ilium, will clear up the diagnosis.

Cysts of the femoral neck may occur, which so weaken the bone as to give rise to coxa vara. Their progress should be carefully watched by means of the X-ray and if improvement does not take place the trochanter major should be tunneled, the cyst cleansed out, and the wound packed. In cases of osteofibrosis of the femoral neck supports should be given, as in cases of tuberculosis, lest coxa vara result. These cases seem to be the result of perverted metabolism, perhaps caused by failure of some of the ductless glands to do their work, and artificial feeding with these glands is being used more or less empirically. Such children are usually remarkably fat and have undeveloped genitalia.

At times **periostitis of the great trochanter** may simulate quite closely hip disease, pressure over the trochanter giving rise to acute pain. If the head of the femur, however, be pressed into the acetabulum by one hand on the middle of the thigh while the knee is abducted with the other, no pain is produced and the sensitive spot is thus located in the trochanter and not in the head of the femur.

The occurrence of **tumors of the femur and ilium** should not be over-

looked. These are almost always sarcomata, and can usually be differentiated from tuberculosis or syphilis by the rapid enlargement of bone usually following quite soon after a traumatism associated with pain, which is usually caused by pressure on nerve trunks and does not resemble in its characteristics the night cries of ordinary hip-joint disease. Muscular spasm is also usually wanting. The importance of a correct diagnosis being reached very early in such cases cannot be overestimated, as it is only by prompt amputation that life can be saved.

A point to be borne in mind in making a diagnosis of abscess in connection with a fluctuating swelling on the buttock is the possibility of confounding one with an aneurism, as there is on record a case of gluteal aneurism that was opened with fatal result under the impression that it was an abscess. It is always best to confirm the diagnosis by aspiration.

ETIOLOGY.—The ordinary accepted type of "hip disease" or "*morbus coxarius*" is a tuberculosis, which in the vast majority of instances begins in the bone, though it may, in exceptional instances, commence in the synovial membrane.

How the tubercle bacilli gain access to the bone is a matter which is still under discussion. It is probable that the bacilli are present in the circulation, and that under the influence of a traumatism, not necessarily severe, a lowering of the resistance is produced in the neighborhood of the joint sufficient to favor the local development of bacilli which have been present in the general system for a long time, but which had not increased on account of lack of suitable conditions.

Tuberculous material was injected by Muller into the femoral artery of animals with negative results. When injected into the crural artery from which the nutrient artery of the femur arises or into the nutrient artery itself, typical bone tuberculosis was set up.

Tuberculous matter from phthisical lungs injected into animals' joints sets up tuberculous joint disease, while injection of inorganic matter not containing tuberculous matter either into the joints or general condition does not cause tuberculosis.

Schüller rendered guinea-pigs and dogs tuberculous by inhaling solutions of tuberculous material from diseased lungs and injected the same into the animals' lungs. The joints of these animals were then wrenched or bruised, which produced a typical chronic tuberculous synovitis in a great proportion of the cases, while healthy animals whose joints were similarly treated suffered from only a temporary sprain. Fraser found that injection of bacilli into the femoral artery did not set up tuberculosis of the knee unless the femoral vein was occluded, but when this was done tuberculosis of the bone invariably occurred.

The exanthemata are frequently followed by joint-tuberculosis—apparently on account of the lowering of the general vitality below the point where the tissues are capable of resisting the growth of the tubercle bacilli.

PATHOLOGY.—In the early stages of hip-joint disease there is a hyperemia in the cancellous tissue about the epiphysis where the disease usually begins, in the center of which a small, gray tubercle appears.

The capillaries in the Haversian canals become blocked up with bacilli. A hyperemia is kept up, the trabeculae in the hyperemic area are absorbed, enlarged bone-spaces are formed, and fatty degeneration of the bone-cells occurs.

The gray spot in the center of the hyperemic area increases in size; its center begins to grow yellow; other similar spots occur and merge into each other; the center breaks down and becomes a semisolid, cheesy mass and may turn into pus.

The blood-vessels in the periphery of the inflamed area often become so blocked that the blood-supply is cut off, and necrosis of a larger or smaller part of the apophysis of the femur results. If all conditions are favorable, the focus may become absorbed or may become calcified, or else as the focus of disease increases in size it may grow toward the surface of the femur, open outside the joint-cavity, and the case may run a comparatively short course with little or no destruction of the joint, or, as is more usual, it may break into the joint itself, setting up a purulent synovitis.

The synovial membrane becomes inflamed and thickened, the blood-vessels are engorged, an increased serous or seropurulent effusion takes place, and the joint becomes filled with a gelatinous mass; the cartilage becomes eroded, and the bare ends of the bone come into contact.

If the process becomes less violent, on the contrary, the granulations become firmer and not so pale and gradually give place to fibrous tissue, adhesions forming between the joint-surfaces, scar-tissue taking the place of the granulations, and contraction of the capsule limiting joint motion.

When the focus of disease is in the ilium, the area of inflammation may advance toward the pelvis as well as toward the acetabulum, and in these cases the periosteum lining of the ilium on its inner side becomes much thickened. At times the entire bottom of the acetabulum may be absorbed and the head of the femur pass into the pelvis; at other times there is only a small hole through which pus passes to form an abscess which may burst into the bladder or rectum or burrow under the adductor tendons or out on the buttock. Even in this condition recovery is not impossible.

The size of the acetabulum is often increased by the progress of erosion and also by the action of reflex muscular spasm in crowding the head of the femur against the upper rim of the acetabulum, cases having been reported in which the head of the bone lay inside the pelvis in spite of the limbs' having been kept parallel by plaster of Paris, which had prevented the occurrence of deformity.

The importance of this fact as bearing on the necessity of traction as well as fixation in the treatment of the disease should not be overlooked.

The erosion of the upper part of the acetabulum accounts for part of the shortening in some cases of hip disease. Retardation of growth may give actual shortening of the femur, and it is not unusual to find that the leg and foot of the affected side are also smaller than their fellows.

If the disease progresses, sinuses may burrow from the joint in all directions both inside and outside the pelvis, and later on amyloid changes in the liver and kidneys will be set up, or a tuberculous meningitis or a general tuberculosis may set in.

PROGNOSIS.—Prognosis in disease of the hip-joint varies very much, being largely determined by the amount of destruction which has taken place before the case comes under observation, the amount of recuperative force possessed by the patient, and the intelligence of home co-operation—the last, perhaps, being the most essential element.

Cases of syphilitic disease ought to give excellent results, if to local protection of the joint be added thorough, persistent antisyphilitic treatment.

Cases of acute traumatic synovitis, if seen at once, and given absolute and complete rest, almost always recover perfectly.

Cases of acute infectious osteomyelitis demand prompt operation and removal of diseased foci. If this can be done before too much general systemic infection has taken place, prompt recovery usually follows.

In tuberculous cases, seen early, recovery, as a general thing, takes place. The time which a patient will have to wear a splint is very seldom under two years. If the patient is able to dispense with it inside of this time, it is remarkably fortunate, and the parent should not be led to anticipate such a result. The amount of shortening which may take place, and the amount of impairment of motion, cannot always be accurately determined beforehand, and it is very unsafe to make a definite prognosis. Cases may be seen at apparently the same time after the onset of the first symptoms, with apparently the same amount of disease, be treated in precisely similar manner, and while one recovers with an absolutely perfect joint at the end of two years, the

other may drag on a tedious course of four, five, or six years, and at the end of that time recover with decided shortening and marked diminution of motion. The only difference in the two cases apparently having been the personal equation of power to resist disease. What can be promised is that, if the patient's recuperative force is sufficient to allow it to recover at all, it can recover with a leg parallel with its fellow, and not flexed upon the trunk, and the parents may be told that the length of time during which a splint will probably have to be employed will not be less than two years.

Abscesses and sinuses always mean a worse prognosis, for there is often nephritis or amyloid degeneration, or tuberculous processes elsewhere, meningitis following hip tuberculosis oftener than in any other joint. Coe (*Med. Jour. and Rec.*, Aug. 5, 1925).

The question of abscess also comes into the prognosis, and parents are frequently anxious to know whether or not a child will have an abscess. In many cases there is felt at the time of first examination a brawny, porky induration around the hip-joint, which is the forerunner of an abscess, or the child may be found with an inflamed, sensitive joint which absolutely precludes any possibility of motion; in such cases it is quite probable that an abscess will develop more or less speedily. In other cases, where the patient is seen early, and the brawny induration is as yet not present, no definite prognosis can be given, though the percentage of cases that develop abscesses when thorough treatment is carried out from an early stage of disease is decidedly small.

TREATMENT.—The indications for treatment in disease of the hip-joint are, primarily, to give the joint physiological rest, and, secondarily, if the general condition of the patient demands special treatment to counteract syphilis, rheumatism, etc., to carry out the measures indicated.

At the Mayo Clinic, the acute stage in children is treated by the **Jones abduction frame**, whereas in adults this stage may be treated by **Buck's extension** in bed, with a sandbag support for the leg. In the subacute stage, in cases without drainage, a **cast** of the Lorenz type may be applied with the use of crutches and the elevation of the sound limb by means of a patten. Finally a **Thomas splint** is used for 3 or 4 months, at the end of which period, when weight carrying is permitted and causes no pain, crutches are allowed. Of his cases 90 per cent. showed deformity, the flexion abduction type being practically always present; 19 per cent. had ankylosis, and the average shortening was $2\frac{1}{4}$ inches. In 60 per cent. the right hip was the seat of deformity, 10 per cent. required **aspiration**, and 14 per cent. required **curettage** or **sequestrectomy**. Patients with deformity and those in the subacute stages were treated by brisement forcé, plaster of Paris, and crutches. **Osteotomy** of the Grant type was done in the cases with ankylosed deformity. H. W. Meyerding (Minn. Med., Aug., 1918).

To obtain rest of a joint like the hip is not easy. The **Thomas hip-splint** endeavors to secure it by fixing the trunk and lower extremity by means of an iron bar $\frac{3}{4}$ inch by $\frac{3}{16}$ inch sufficiently long to extend from the scapula to the lower third of the calf and fitted with cross-bars long enough to embrace three-fourths of the circumference of that part of the body where they are placed, namely: at the thorax, calf, and upper third of

the thigh. The splint is padded with felt, covered with leather and bent to fit the contour of the body in its deformed position, and then bandaged firmly to it. In acute synovitis of the hip it is an excellent means of treatment, and in cases where no other form of treatment is practicable is capable of doing much good. The fixation which it gives the hip, however, does not counteract the reflex muscular spasm which in chronic joint disease creates so much of the destruction which is seen in cases left to nature, and which is capable of causing perforation of the acetabulum in cases that have been simply prevented from having flexion, but not treated with traction.

Fixation can also be given tolerably well by a **plaster-of-Paris spica** to the thorax, but the practice of permitting children with inflamed hips to walk on such limbs in plaster spicas is unwise and more apt to result in ankylosis than when the traction splint is employed.

Traction in the proper line and of sufficient amount to relieve involuntary muscular spasm and so lessen intra-articular pressure is the best agent we possess for relieving pain in chronic joint disease, and should always be added to any apparatus that is employed for securing fixation, as the latter, unless thus supplemented, but partially fulfills its mission.

Another objection to the Thomas splint is the method by which it straightens the deformity, which is effected by bending the splint backward by wrenches from time to time. If there is contraction of the flexor muscles, this proceeding must result in crowding the head of the bone vio-

lently against the acetabulum, thus running the risk of re-exciting inflammation.

In the majority of cases there is too much deformity when they first come under observation to permit the application of a splint. Such patients should be put to **bed, a long padded side-splint, with a cross-bar at the bottom**, should be firmly bandaged against the sound leg and the trunk as far as the axilla, and the **body and leg** thus secured may, if necessary, be **fastened to the sides of the bed** for the purpose of retaining them in position.

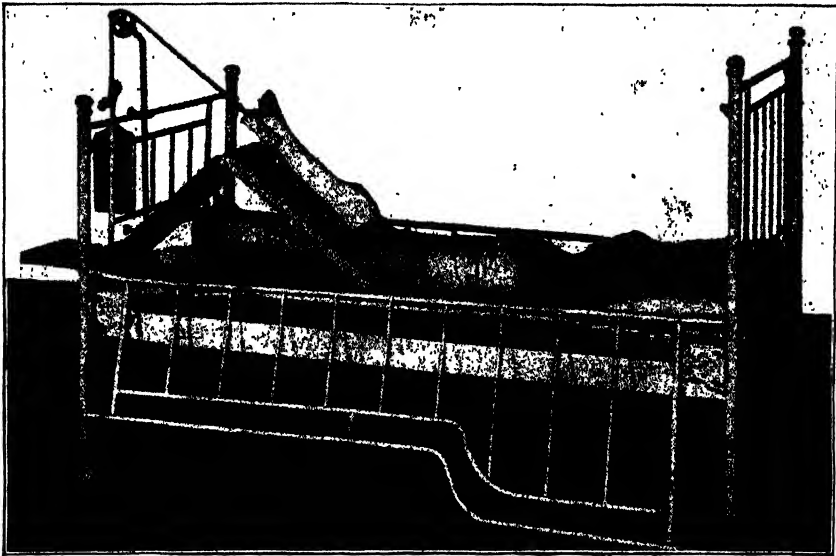
The first essential is **rest in bed** with sufficient **traction** to overcome the pull of the muscles. The traction must be at first in the line of the deformity, whether this be toward the foot of the bed or over the shoulder. When spasm has passed off, the direction of traction is changed slightly toward the normal, and this is continued at intervals until the leg is straight beside the other, always waiting between changes of direction until both adductor and flexor spasm have completely disappeared, whether this be days or weeks. After 1 or 2 months in the normal position to permit continued healing, the patient is ready for a splint, preferably the **Bradford traction abduction splint**. This consists of a ring which rests against the perineum, the ischial tuberosity and the outside of the hip above the trochanter, with a short projection which holds the leg in slight abduction. To the ring are attached 2 rods terminating well below the foot and carrying a small ratcheted bar to which may be attached the straps of an ordinary Buck's extension, adjustable, by turning the bar, to any desired degree of traction. The object of this splint is to enable the child to become ambulatory at the earliest possible time, and thus develop health and resistance through general muscular activity. Immobilization, although not absolute, is sufficient for healing;

ankylosis is prevented, and resulting function is usually excellent. The Massachusetts Hospital School, using this method, has completely discarded the former treatment by plaster without extension. The duration of bed treatment is 3 to 18 months, and of ambulatory treatment usually 2 to 3 years, the splint being removed at night during the last 5 or 6 months. With the cast method the course is longer than necessary and the records usually show frequent acute exacerbations, while under the treatment described the period of disability is much shorter, exacerbations have not occurred, and function in most cases is excellent. H. E. Coe (Med. Jour. and Rec., Aug. 5, 1925).

It is sometimes found better to bandage the patient with **Bradford's frame**, a rectangle of iron gas-pipe somewhat longer and broader than the child, which has canvas stretched tightly across it except at the part where the hips lie, which is left open for a bed-pan. A long board should be placed under the mattress, as the ordinary spring-mattress is too yielding to allow proper control of an inflamed joint. **Adhesive-plaster straps**, furnished with buckles at one end, are next applied to the diseased limb, the buckles being just above the malleoli, and the plaster extending as high on the thigh as possible. Heavy extension **diachylon plaster**, spread on mole-skin, is best for this purpose, as the ordinary rubber plaster is irritating to many skins when worn for a long time, and is spread upon such thin cloth as to be incapable of enduring the strain necessary in many cases to afford relief. In applying the plaster it should be warmed but very little, and in many cases need not be warmed at all, but should be snugly bandaged to the skin, and well rubbed with the hand to secure coaptation of

the plaster. This tight bandage may then be removed and replaced by one not so closely bound. Some prefer, in addition to the two side straps of plaster, a spiral of plaster passing around the leg in both directions, which serves to hold the plaster more snugly in position. Properly applied extension plasters should remain for several months without the necessity of change. To the buckles are now

When the body and sound leg are firmly bandaged to the side-splint and the back is flat upon the bed, the diseased limb will assume a position either of abduction or adduction, combined with flexion, and in this position, whatever it may be, the line of **traction** must be made. The amount of traction must be made sufficiently great to give the patient freedom from pain. If traction, so applied,



Extension apparatus.

attached small leather straps, which are fastened to a cross-bar below the sole of the foot, from which cross-bar a stout cord extends over a pulley-wheel at the foot of the bed and supports a **weight**. The amount of weight will vary in different cases, and should be that which experience shows gives the greatest amount of relief in the particular case, and may vary from 2 to 15 pounds. The direction in which the traction is made should be determined by the deformity which is present in each particular case.

fails to relieve pain, and the position is that of adduction, a **second line of traction** may be made by passing a well-padded band around the thigh, close to the groin, and making traction **outward** at right angles to the long axis of the femur, over a pulley fastened to the side of the bed. The **leg** must be **supported** in its elevated position by pillows or by two boards hinged at one end and supplied with a prop, so as to make an **inclined plane** which can be raised or depressed according to the needs of the patient. If there is great tenderness behind

the trochanter, a **blist**er may be applied with great benefit.

In cases of osteitis of the trochanter with marked tenderness, relief can frequently be obtained by plunging the sharp point of **Paquelin's cautery** deep



Long traction hip-splint with thorax belt. (Sayre.)

into the bone, the skin over the trochanter having been anesthetized by a few drops of a 1 per cent. solution of cocaine. In exceptional cases there may be an effusion in the joint of so great extent as to make **aspiration** advisable, but this is unusual. If the synovitis becomes purulent the joint must be **incised** and washed out with **Thiersch** or **chlorinated soda** solution.

The **line of traction** is to be **changed** little by little **every few days**, as the spasm of the muscles subsides, until the leg is gradually brought parallel to its fellow and flat in bed, without disturbing the position of the trunk and the sound leg. When the legs can be made parallel and rest on the bed without tilting the pelvis, a **splint** may be applied. In some cases the disease will have advanced so far at the time of first observation that adhesions will have formed around the joint too strong to permit reduction of the deformity in this manner. And in such cases, where faithful trial of this method of reducing the deformity fails to give results, the patient should be anesthetized and the **joint forcibly straightened**. If at this time it is found that there is so much contraction of the rectus muscle or the adductors as to prevent reduction of the deformity, except at the expense of violently crowding the head of the femur into the acetabulum, **free section** of the **contractured tissues** should be made before reduction is attempted. The joint should then be **immobilized** either with a splint or with a plaster-of-Paris dressing extending from the ankle to the thorax, while **weight-and-pulley traction** is again resumed. If plaster of Paris is employed, it should be reinforced at the groin by a strip of iron or bass-wood to prevent cracking. When the deformity has been overcome and the joint is free from active inflammation, the patient may be allowed to rise when supplied with a suitable apparatus.

The object of the **hip-splints** now in use is twofold: First, to enable the patient to walk about easily without bearing weight upon the diseased

joint, and, second, to prevent the joint from receiving the traumatism consequent upon ordinary motion. If the patient is very large and fat or the joint extremely sensitive, it will be found wise to use a pair of **crutches** in addition to the hip-splint, as the joint in this manner will be better protected and the patient freed from the galling sometimes occasioned by the pressure of the perineal straps in very heavy and fat patients. In the great majority of cases the apparatus most suitable for protecting the joint consists of a **thorax belt and a pelvis belt with a bar running down the outer side of the leg** to a point a couple of inches below the sole of the foot, where it joins a cross-bar, to which are attached two straps, which serve to fasten the instrument to the buckles on the adhesive plaster. By means of a ratchet and key on the footpiece which is attached to a notched bar sliding inside of the main bar, which is hollow, the splint may be made longer or shorter. Just above the knee a metal horseshoe-shaped collar holds the thigh in position. Two straps pass from the front of the pelvis belt to the rear, between the legs, and serve to hold the pelvis belt in position. The buckles to which these straps are attached should be near together in the front, to avoid pressure on the femoral vessels, and widely separated at the back in order that the pressure may come under the tuberosity of each ischium.

An elastic strap runs from the middle of the back bar of the pelvis belt to the side rod to prevent the pelvis belt from tipping up too far in the back. When applied the pelvis belt is to be fastened sufficiently firm by the perineal straps to prevent it

from rising higher than the antero-superior spines of the ilia, while the footpiece is buckled to the extension straps, leaving $2\frac{1}{2}$ to 3 inches between the sole of the foot and the top of the footpiece. By means of the ratchet and key extension is then made until the patient is comfortable. As the splint projects below the level of the foot, an extra sole and heel must be added to the shoe of the opposite side, which should usually be about 4 inches high, and the splint should be so regulated that, when the proper amount of traction is made, the patient being upright, the length of the splint and the length of the sound leg with the high shoe will be the same. The splint should be sufficiently long to prevent the patient from touching the foot to the floor, and, if the elevation on the opposite shoe is not high enough to compensate for this elongation, walking will be very uncomfortable. In the majority of cases a splint of this kind gives adequate protection and results in excellent cures. But if it is found that the parents do not fully understand the home management of the apparatus, or if the patient lives at a distance, so that it is seen at infrequent intervals, it may be wise to **add to the splint a thorax belt**, which is joined to the pelvis belt by means of a rod continuous with that passing down the side of the leg. This form of splint prevents the occurrence of flexion after the patient is allowed to walk, which sometimes takes place if there is no thorax belt on the splint, but it has the disadvantage of limiting the motions of the patient very materially, and being much more cumbersome. With the patients, however, who live at a distance, and where home co-operation

is not intelligent, it is wise to employ it. The mistake must not be made of placing a joint in the bar that runs from the foot to the thorax belt, as this will render the apparatus worthless. In some cases, also, instead of the perineal bands, it may be better to use a ring, as suggested by Dr. A. M. Phelps, for the latter cannot be tampered with by careless attendants, and, if it is fitted to the limb with proper care and sufficiently well padded, can be used with a fair degree of comfort. In adult cases where dependence can be placed upon intelligent co-operation of the patient, the use of the **short traction splint and crutches** may be advisable. In this form of splint the side rod terminates at the knee-joint and is joined to a pair of hoop-shaped metal bars, which pass across the front of the femur and are supplied with two jaws on each side of the knee just above the condyles. Adhesive plasters are fastened to the thigh, terminating in broad, webbing bands, which are reversed over the jaws of the splint and fastened to buckles. By means of a ratchet and key traction on the joint is made in the same manner as in the case of the long splint.

The treatment of abscesses occurring in tuberculous joints is one which has been very widely discussed, and in regard to which there have been many different opinions. The prevailing trouble with many surgeons is that they fail to regard the abscess as an incident in the career of a tuberculous joint, and treat it as a thing by itself, neglecting the bone inflammation which was the original starting point of the abscess. If it were possible to locate the focus or foci of disease and to remove all foci

without doing great damage to surrounding healthy parts, the logical treatment of all tuberculous inflammation would be the radical **excision of all tuberculous foci** as soon as detected. This proceeding, indeed, became quite fashionable some years ago abroad, but experience has shown that better results are obtained by older and more conservative methods. If we cannot absolutely eradicate all tuberculous foci, the chances of securing a good result are better by leaving them alone, provided they remain encapsulated and are not subjecting the patient to general systemic infection. Under **rest and compression**, good **hygienic surroundings**, and **forced feeding** many collections of tuberculous matter disappear. If they come to the surface it is the best plan in many cases to **disinfect the skin** with great thoroughness, apply a **sterilized dressing**, and **allow them to open spontaneously**; **wash the cavity** thoroughly with **hydrogen dioxide or chlorinated soda**. Abscesses treated in this way rarely give rise to any disturbance and usually close in a few months.

In the treatment of abscess formation the general principle is to avoid secondary infection whenever possible, which means **incision** only when general and local measures, such as feeding, hygiene, local heat and **aspiration** are unavailing. When sinus formation has occurred, unobstructed **drainage** is the first essential, and this may be supplemented by local applications or injections of various kinds, by **hyperemia** induced by the method of Bier, by **hypertonic solutions**, by **heliotherapy** or other forms of radiation, or by **dry heat**; also, perhaps, the use of **vacuum** in selected cases to combat secondary infection. The operative procedure of extensive removal of diseased bone, often including large portions of the

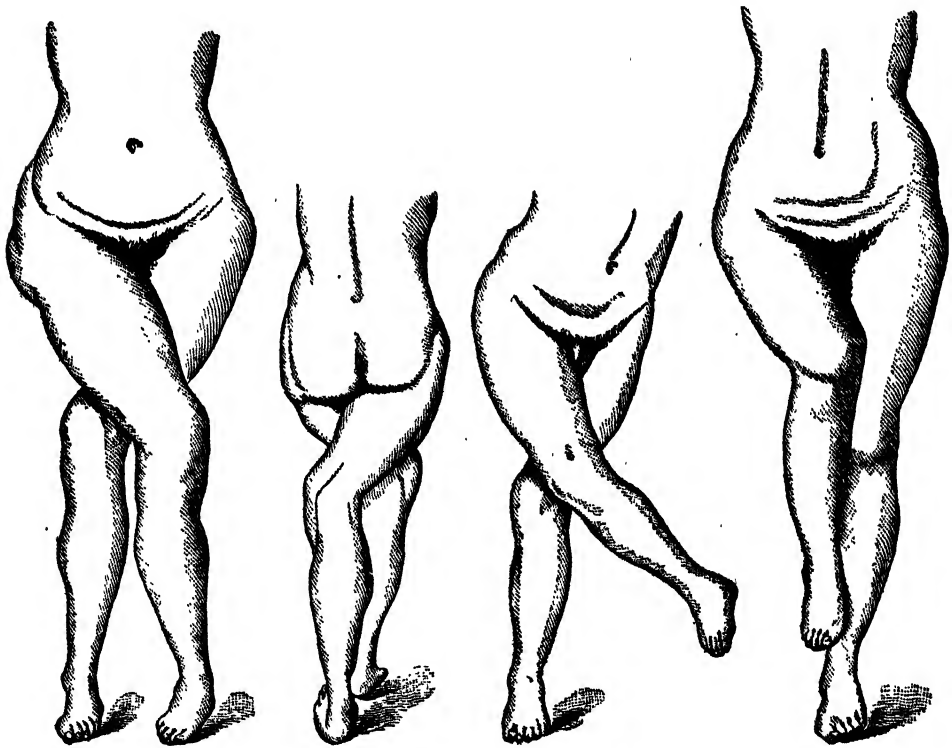


Comparison between tuberculous and healthy hip-joints, showing absorption of the head and neck of the femur, rarefaction of the head, and absorption of the acetabulum. Normal side shows epiphyseal cartilage below the head of the femur and cartilage in the acetabulum, where immature bone has not yet ossified. Bandages and adhesive plasters show on thigh of diseased side. (*Sayre.*)

head or ilium, should be reserved for the most advanced cases of hip disease. H. E. Coe (Med. Jour. and Rec., Aug. 5, 1925).

If there has been a mixed infection grafted on top of the original tuberculous focus, immediate operation with **free incision of the abscess**, complete

Many cases pass on to abscess quite promptly, and, indeed, it sometimes seems as if those cases which suppurated early and ran an acute course got well in shorter time than those which were accompanied with less pain and less suppuration. The occurrence of abscess does not neces-



Deformities following hip-joint diseases due to insufficient care during treatment. (Petit.)

removal of all *débris*, and thorough drainage should be employed. As a usual thing, the abscess has originated in the bone, and in the cavity will be found very frequently some crumbs of dead bone, although occasionally they are not present, while not infrequently, in cases opened at an advanced stage, the abscess seems to have been shut off from the original bone focus, which has healed up after extruding its carious bone.

sarily mean a less favorable result, and it is not unusual to see cases of double hip disease, one side having been the seat of an abscess and the other having been free from suppuration, in which the motion is better on the side where suppuration took place.

If great destruction of the head of the femur or the acetabulum are present when the case first comes under observation, or if, in spite of protection and good hygienic sur-

roundings, the case does not do well and disintegration of the joint is progressing, the question of **excision** presents itself. And here again the difficult problem is when to operate and when not. The great majority of cases seen in the early stages and properly treated never reach the point of operation, except in the class of acute infectious osteomyelitis. And, again, there are other patients who come to the surgeon with grave hectic symptoms, a hip full of burrowing sinuses, and a mass of dead bone inclosed in a thick involucrum, who have no chance for life except by the prompt removal of all diseased tissue and proper drainage.

Pain and disability of the left leg in a child of 3 years were found due to a small tuberculous focus in the trochanteric region, without involvement of the femoral head or acetabulum. Severe hip-joint disease was averted by removal of sequestra and fungous tissues in the tuberculous cavity, by curettage and injection into the cavity of 5 c.c. of a suspension of iodoform in oil. After closure the leg was placed in plaster in slight abduction. With added general treatment and heliotherapy, the patient was practically cured. Early X-ray diagnosis is necessary in such cases in order that the disease focus may be removed before it has perforated into the joint. E. Allenbach (Rev. d'orthop., July, 1924).

Between these two extremes we find a third class, in which the surgeon at times is in doubt whether the continued use of a splint for a longer period of years is better, or whether a free removal of the head of the bone, scraping of the acetabulum, and removal of all tubercular tissue may not, in the end, give a better result. Such cases must be decided by each man on his own experience.

Roberts succeeded in reconstructing a tuberculous hip-joint so as to eliminate the disease and furnish a new and apparently serviceable head on the femur, by using an astragalus removed from the patient's own foot. This operation of **transplantation** was suggested by an astragalus which had been removed from a paralytic foot, and which showed striking similarity of contour, when held in certain positions, to the head and neck of the femur, and presented so large an articulating surface that it seemed possible to use a portion of the bone as a graft to replace the femoral head. By this operation the period of treatment could be reduced to 4 or 5 months. The half-destroyed head of the femur was freed and sawed off at the middle of the neck. An ivory pin, 1 inch long and $\frac{3}{16}$ inch in diameter, threaded its whole length, was then screwed into the stump of the neck and the semi-spherical piece of astragalus was screwed down hard on the cut end of the femur. The newly formed head was replaced in the acetabulum. After 10 weeks the graft was found united with about 30 degrees of voluntary motion.

In 2 cases of tuberculous coxitis the writer, to combat the demineralization shown by fluoroscopy, introduced a **bone and periosteum implant**. A bar of bone tissue, taken from the tibia, was driven through the neck, head and cotyloid bone. Radiograms of the cases taken 4 years later testified to the favorable and definite results obtained. Maragliano (Riforma Medica, May 17, 1919).

An **abducting traction splint** is much to be preferred to the plaster spica bandage in tuberculous hip disease. When the carious process is healed with marked deformity and bony ankylosis, the best treatment is **subtrochanteric osteotomy, correcting flexion**, and placing the limb in an **abducted position**. In severe cases of active tuberculosis with acetabular involvement, the hip can be **forcibly dislocated** by open **incision** (in order to relieve the acetabulum of pressure), the lesion **drained**, and the deformity corrected later. Bradford (Surg., Gynec. and Obst., Dec., 1921).

Out of 179 cases of hip tuberculosis treated from 1899 to 1920, 78 were operated upon. The operations included, aside from **sequestrotomy**, **scraping out of sinuses** and **opening of abscesses**, 6 cases of **resection of the femoral head**, a like number of **resection of the whole joint**, 2 of **subtrochanteric osteotomy**, and 1 of **resection of the femoral neck**. Tracing 26 of these cases, 3 were found to have died 3, 9 and 12 years after operation. Nineteen were completely cured; 3 had recurrences, the sinus not healing until after repeated operation. None were required to wear orthopedic shoes or use a cane in walking. N. Antelawa (Arch. f. klin. Chir., Aug. 7, 1924).

Arthrodesis is probably the best solution for the adult patient with a tuberculous hip-joint. It is not so easy to obtain as in the knee, and this, with the technical difficulties, explains why the operation is not in favor. In children the treatment should be essentially conservative. Eighteen patients were subjected in 1 year at the Mayo Clinic to surgical procedure, such as correction of bad position by **brisement forcé** and the application of a **cast**, to **aspiration** and injection of abscesses, or to arthrodesis. M. S. Henderson (Jour.-Lancet, Aug. 15, 1924).

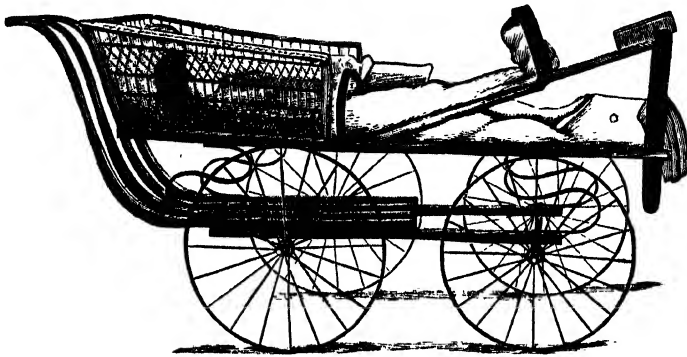
Case of a man aged 28 who had had tuberculosis of the right hip with supuration when he was 4 years old. There was complete destruction of the head and neck with upward displacement of the trochanter, resulting in a shortening of 5½ inches. Prior to operation **traction** was applied, the trochanter being pulled down 2 inches. At operation, a small amount of bone was chiseled up from the upper rim of the acetabulum and a new acetabulum reamed out from the thickened part of the ilium at that point. The upper end of the femur was placed in the new acetabulum and the trochanter brought down on the outer side and sutured. A **long plaster spica** was applied with the limb in 25 degrees of abduction. After 8 weeks the long spica was replaced by a **short spica**. When this was removed

at the end of 12 weeks, **active and passive motion** and physiotherapy were begun. Muscular tone of the atrophied limb was markedly restored, the shortening reduced to ½ and the patient enabled to walk with a cane, with a fair amount of motion. W. L. Sneed and R. H. Patterson (South. Med. Jour., Nov., 1925).

In case operation is decided upon, if the patient has a large abscess and is very much exhausted it is usually better to **open the abscess freely** and **wash it out** at one sitting, and in a few days, when the patient has rallied from the removal of retained pus, to complete the **clearing away of dead bone**. Except in cases presenting many old sinuses, where it sometimes is best to unite these by an incision, the best method of reaching the joint is by an incision starting midway between the anterosuperior spine of the ilium and the greater trochanter, and, passing over the great trochanter, down the thigh along its outer aspect. This incision should pass completely through the periosteum and extend to a point below the lesser trochanter. By means of a curved bistoury the periosteum should now be divided at right angles to the original cut and, by means of a periosteal elevator, peeled up from the femur. At the digital fossa it will be necessary to resort to the knife to divide the muscles inserted there. At all other points the periosteum can be peeled off by the periosteal elevator. The **femur** should be sawed just above the lesser trochanter, and the **head removed** from the socket by means of a pair of lion forceps, or it may be dislocated from the acetabulum prior to sawing, at the pleasure of the operator. If there are evidences of disease farther down the

shaft of the femur the periosteum must be split lower and the femur sawed in two lower down. The acetabulum should then be explored, and, if any foci of disease exist, they should be carefully removed with a sharp spoon. If the acetabulum is perforated, the opening must be enlarged so that no shoulder of bone shall cause pus to accumulate in the pelvis. Sometimes it is necessary to **drain** such **intrapelvic abscesses** through the **sciatic notch** instead of

limb is then fastened to the footboard of the cuirass by means of adhesive pieces extending to the thigh, as for the application of a hip-splint, and the footboard is then drawn down until both legs are of the same length, the bandages just mentioned as passing between the legs keeping the trunk from slipping down. The patient can be dressed in his cuirass, which is cut away under the buttock for this purpose, with much less pain than in any other manner, and can



Light carriage for cases in which recumbency is unavoidable. (Bremner.)

the acetabulum. If any **sinuses** exist, they should be **carefully cleaned** and all **tuberculous tissue** removed as far as possible. The **wound** should then be thoroughly **packed** from the bottom with **balsam-of-Peru gauze** and the patient placed in a wire cuirass. The **wire cuirass** consists of a wire framework extending from the head to the heels, with a pair of movable foot-pieces, which allow the legs to be lengthened or shortened. The **sound leg** and the **trunk** are firmly **bandaged in position** by a roller bandage. Turns of the bandage also pass over cotton pads in the groin and around the handles of the cuirass and serve to give **countertraction**. The diseased

have the benefit of outdoor life from the time of operation, being transported in a wheeled carriage.

If a cuirass cannot be had, a **double Thomas hip-splint** will answer the purpose if **combined with traction** by weight and pulley. The wound should be dressed as frequently as may be necessary to keep it clean, the packing gradually being removed as new bone regenerates from the inner surface of the periosteum, and in some cases nature will form an artificial joint almost as perfect as its fellow, although this is not to be expected, and a certain amount of shortening and more or less disability usually result.

Cases of double hip disease must be treated by **rest in bed** or by the use of the **cuirass**, as it is not possible to apply an apparatus which will allow them to walk in a convenient manner and still protect the joint.

The same rules apply to the adult as to the child, but are more difficult to put into practice, and often bed treatment is better than an ambulatory splint, but, if possible, this **bed treatment** should be **out of doors**. This holds true of all bed treatment.

In exceptional cases **amputation at the hip-joint** may be a necessity to save life, but this is most uncommon, recovery with a most excellent joint on which the patient walks well having been reported by J. C. Spencer after removal of 9 inches of femur.

If amputation is done, Fernaux Jordan's method should be employed.

REGINALD H. SAYRE,
New York.

JUNIPER.—Juniper consists of the fruit (berries) of the *Juniperus communis*, of the family Coniferae, a small evergreen tree of Europe, North America, northern Africa, and Asia. The berries are about $\frac{1}{8}$ to $\frac{1}{4}$ inch in diameter, dark brown or purplish in color, possess a sweet and resinous taste, and contain 0.5 to 2 per cent. of a volatile oil, upon which their medicinal effects chiefly depend, a non-crystallizable principle (juniperin), a resin, from 15 to 30 per cent. of dextrose, etc. The volatile oil also exists in the leaves and other parts of the plant, and by first bruising and then macerating them in alcohol or spirit the liquor commonly known as gin is produced. The oil of juniper obtained from the wood is inferior to that distilled from the berries, which is the official form of oil.

Oleum cadinum, U. S. P. (oil of cade; juniper-tar oil), obtained by destructive distillation from the wood of *Juniperus oxycedrus*, is a thick, brown, empyreumatic oil resembling and having the odor of tar, and

with a warm, faintly aromatic, bitter taste. It is very slightly soluble in water, but imparts to it an acid reaction shown by moist blue litmus paper. It is only partially soluble in alcohol, but is completely soluble in 3 parts of ether. Juniper tar contains (1) hydrocarbons which form its greater part; (2) acetic acid and its homologues; (3) phenols and allied bodies, and (4) resinous substances. It is poorer in phenols than tar from the pine or aspen, and has less disinfecting power than the other tars.

PREPARATIONS AND DOSE.—*Oleum juniperi*, U. S. P. (oil of juniper), consisting of terpenes (pinene and cadinene) and juniper camphor, and occurring as a colorless, greenish, or yellow liquid with characteristic odor and aromatic, slightly bitter taste, soluble in 4 volumes of alcohol and in ether. Dose, 1 to 10 minims (0.06 to 0.6 c.c.); average, $1\frac{1}{2}$ minims (0.1 c.c.).

Spiritus juniperi, U. S. P. IX (spirit of juniper), made by mixing 1 part by volume of oil of juniper with 19 parts of alcohol. Dose, $\frac{1}{2}$ to 1 fluidram (2 to 4 c.c.).

Spiritus juniperi compositus, U. S. P. IX (compound spirit of juniper; gin), a mixture of 8 parts by volume of oil of juniper, 1 part each of the oils of caraway and fennel, 1400 parts of alcohol, and water, enough to make 2000 parts. Dose, 1 to 4 fluidrams (4 to 15 c.c.).

An infusion of juniper, made from 2 drams to 1 ounce (8 to 30 Gm.) of juniper berries, in 1 pint (500 c.c.) of water, is also sometimes used, the entire amount being administered in twenty-four hours in divided doses.

PHYSIOLOGICAL ACTION.—The diuretic action of juniper is due to a stimulating effect upon the renal structures, which may reach irritation when the drug is administered in excessive doses. Anuria may thus be induced. These effects are produced by the volatile oil, which, first absorbed into the general system, is then eliminated through the kidneys. The oil also exerts a stimulating action upon the gastrointestinal tract.

POISONING.—In overdose juniper produces an irritant action on the gastrointestinal canal and upon the genitourinary tract. Its action upon the latter may result in strangury, priapism, hematuria, suppression, and uremic intoxication. A violet-

like odor may be detected in the urine. A rash like that following the use of *copaiba* is sometimes noticed.

Treatment of Poisoning.—If the patient is seen early, the stomach should be washed out through a **stomach-tube**, and **diluent** and **demulcent drinks** used freely. Administration of an **enema of laudanum**, or of **morphine** by hypodermic injection, will relieve the earlier symptoms, while **stimulants** will avert collapse.

THERAPEUTICS.—As a stimulant and antiseptic to the genitourinary tract juniper has long been considered of value, *e.g.*, in **chronic nephritis**, **chronic pyelitis**, and **chronic catarrhal cystitis**. Active acute inflammation contraindicates its use. In the later stage of **scarlatinal nephritis**, when reaction has set in and the renal secretory apparatus is in an atonic condition, it may be of service.

Juniper is a somewhat serviceable remedy in various forms of **dropsy**. An infusion of the berries (1 ounce to the pint—30 Gm. to 500 c.c.—of boiling water), with the addition of ½ ounce (15 Gm.) of potassium bitartrate, may be given daily in chronic Bright's disease; it tends, if anything, to relieve the edema and effusions which are incident to this disorder.

The following diuretic combination is advised by Debove, Pouchet, and Sallard:

R *Olei juniperi* gtt. xxx.

Extract of juniper berries,

Oxymellis scilla

(N. F.)āā ʒiiss (10 Gm.).

Alcoholis diluti ʒiiss (100 Gm.).

Syrupi aurantii ʒiij (90 Gm.).

M. Sig.: Two to three tablespoonfuls a day.

As a diuretic agent for young children, Vogel has recommended 2 to 3 teaspoonfuls of the juice of juniper berries.

Juniper preparations will give relief in the lumbar pain, or sensation of weight across the lumbar region, so frequently experienced by aged persons, in periods of diminished renal activity due to subacute congestion of these organs. **Prostatorrhoea** and the purulent discharge of **gonorrhoea** in its later stages are generally benefited by juniper in moderate doses.

In **gastrointestinal disorders** juniper is useful in small doses as a stomachic and

digestive tonic. A few drops of the compound spirit in hot water will relieve the **flatulence** and pain of **infantile colic**. Gin has been a favorite domestic remedy for pain associated with **menstrual disorders**. A few teaspoonfuls of it in hot water, combined with the external application of heat, frequently give prompt relief. Externally, the oil of juniper, diluted with some bland oil, may be used as a liniment. **S.**

JUVENILE ENDOCRINOPATHIES.—Under this heading are reviewed certain disorders which may clearly be attributed to deficiency of the various endocrin organs. While these structures influence more or less all diseases, in the light of my views, each organ has a distinct pathology of its own, which manifests itself when it becomes functionally inadequate. Various of the more important diseases of this type have been considered under special headings, *e.g.*, **acromegaly** and **Addison's disease**. Besides these, there are disorders which specifically impair the developmental processes of the child, including, in most instances, the mind. (Mongolian idiocy, however, is considered under the **PSYCHOSES**, Vol. VII.)

It should be clearly understood in this connection that, while my interpretation of the functions of the endocrins enables us to understand the *modus operandi* of each morbid process, the phenomena observed include the secondary effects due to other glands with which the impaired organ—impaired through local lesions of its secreting structure or of secretory nerves—is functionally related. These mutual relations will be summarized as each disorder is described.

CRETINISM.

DEFINITION.—Cretinism, or infantile myxedema, is due to deficient

or virtual absence of thyroiodase, the secretion of the thyroid gland, which secretion, by raising the thermogenic activity of the lecithin in all tissues, including the brain and nervous system, sustains metabolism therein. Cretinism, therefore, is the symptom-complex of inhibited metabolism. (Author's definition.)

SYMPTOMS.—These consist mainly in more or less idiocy, stunted growth, and the cretinic facies. Early in the history of the case there is, as a rule, enlargement of the tongue and lips, myxedematous swelling, which seldom appears before the first year (a fat baby being, in some instances, a myxedematous baby), delay in learning to speak and walk, dryness and scaliness of the skin, coarseness of the hair, a squatty or "saddle" nose, scantiness of the eyebrows, puffiness of the lids, and a prominent abdomen or "pot belly."

In severe cases, the child reminds one of an aged person, being wrinkled and yellowish.

The thyroid is enlarged and goitrous in severe cases, but not always in the hypothyroid type, in which it may be hardly discernible. The teeth, which may be represented by but a few sharp points, are irregular and tend to decay early. Backwardness in learning to walk and talk, and the enlarged tongue, which interferes with respiration when the child is in the recumbent position, are striking features, adenoid vegetations and enlarged tonsils often increasing the respiratory difficulty. Thick pads in the supracapsular regions are also reliable diagnostic signs.

The mental state of the child depends upon the severity of the case. In some it is not far removed from that of the "human plant," as Roesch described

such a case. The child fails to recognize its parents or any other person from an object, even toys. It neither weeps nor laughs. It is absolutely apathetic, and sits quietly without manifesting any special wants. It may, however, show signs of hunger or thirst, either by crying like an infant or by grunting. In the higher grades, a few words may be spoken; there is recognition of the parents and familiar faces, and some sign of affection shown for them, but beyond a very limited vocabulary no progress is made. Still higher grades of cretins may speak fairly well, be free in their movements, but fail to develop thereafter.

While thyroid stigmata should predominate in view of the classic conception of the disease, the actual condition is one which entails secondary involvement of the other ductless glands, owing to the deficiency of the thyroiodase supplied by the thyroid to sensitize the phosphorus of the lecithin in all tissues, including that in the cerebral cells. Clinical experience has shown that as soon as this is supplied by administering thyroid gland, the functions of the body are resumed, unless it is administered after irremediable organic changes have occurred.

"Thyroid stigmata," therefore, mean the effects that the absence of sufficient thyroid secretion awakens by passively inhibiting the functions of the other ductless glands.

The basal metabolism makes it possible to ascertain definitely the presence of cretinism, though the facies is so typical that the diagnosis is readily made. Yet some doubt may exist, particularly in fat, chubby children suffering from the larval form of the disease. The basal metabolism is

invariably low, *viz.*, from — 15 to — 45. The figures obtained also afford an idea of the dosage of thyroid preparation which will best meet the needs of the case.

It should be remembered, however, that, in the light of my views, the thyroid hormone does not raise the metabolic rate directly, but does so indirectly by increasing the vulnerability to oxidation of the lecithin in all tissues, originally derived from the adrenals.

Defective oxidation due to inadequate sensitization of the tissue lecithin is well shown by the subnormal temperature, the cold surface, the marked diminution of nitrogen excretion, and the low-blood pressure, the heart and blood-vessels having a lowered tone.

As a result of general vasodilation and low tension, the peripheral circulation is deficient and pallor ensues, the myxedema being in part due to infiltration of the lymphatics of the skin. All muscular elements being likewise deficiently supplied with their thermogenic activator, the muscles in general are ill-nourished and flabby. A similar condition of the intestines practically prevents peristalsis, with inveterate constipation as result, and occasional outbursts of foul diarrhea to relieve the situation.

Deficient activity of the lecithin, due to inadequate excitation by the thyroid hormone, on the osseous system is well shown by the defective development of the bones, the saddle-back nasal bones, the stunted growth, the tardy closure of the fontanels, the lordosis, and the distortions of the limbs. The hands are broad, spade-like, and the fingers pudgy and stiff, a condition reproduced in the feet, the toes of which are more or less kept

apart by the thickened, myxedematous skin.

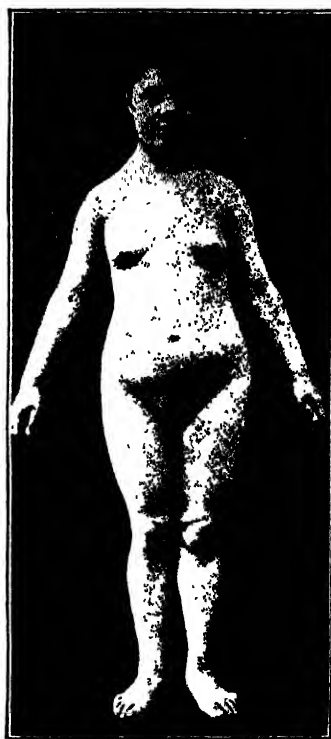
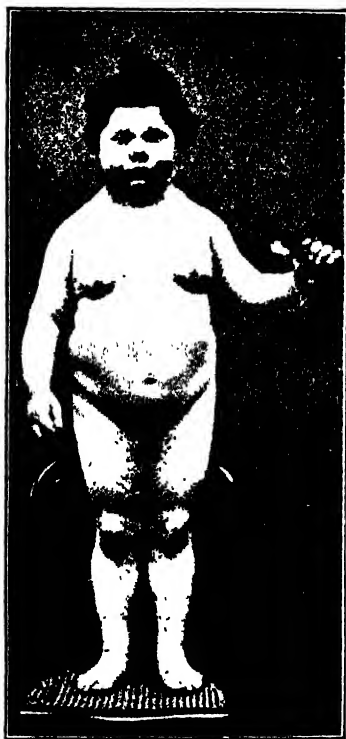
ETIOLOGY.—It is necessary in this connection to recognize 2 types. The first of these, *endemic* cretinism, is often a family disease, and observed in groups in certain localities. It is believed to be due to some chemical substance or micro-organism peculiar to the waters available in those regions. *Sporadic* cretinism occurs in an isolated manner or scattered in any country or region, and in families otherwise healthy.

The so-called "sporadic cretinism" found in the United States differs from that of Europe, and is really an intense, exaggerated form of hypothyroidism which should be known as childhood myxedema, or myxedema in children. Furthermore, out of the 340 cases reported in American literature, only 4, according to the writer, were of the congenital myxedematous type; 31 were of the juvenile type. M. B. Gordon (Endocrin., Mar., 1922).

An important type, too often overlooked and which might be termed *secondary* cretinism or *infantile myxedema*, is mainly due to some lesion of the thyroid caused by an acute febrile disease or some intoxication capable of inhibiting or arresting its functions either before or after birth. From my viewpoint, these factors cause the disorder by initiating organic lesions in the glandular tissues through hemorrhages, autolysis, etc. These areas leading to the formation of fibrous tissue areas, cirrhotic atrophy occurs sooner or later, limiting correspondingly the functions of the organ. Many backward children who are fat and indolent owe their condition to functional torpor of the thyroid caused in this manner, and show prompt improvement when **dried thyroid** is administered to them in small doses.

PATHOLOGY.—Cretinism, in the light of the functions I attribute to the endocrin organs, means deficiency of the product of the thyroid gland proper, its thyriodase. The latter being the physiological activator of thermogenesis and through this, the accelerator of cellular metabolism, deficiency of thyriodase means slow-

myxedematous infiltration; the skin, by its dryness and scaliness, due to inactivity of the sweat-glands, yellowness, etc.; the hair, by its coarseness and dryness; the brain, by the mental torpor, sometimes reaching total idiocy; the muscular system, by enteroptosis, the abdominal muscular relaxation causing pot-belly, flat feet, etc.



Physical development of a cretin under thyroid treatment. (*Lévy and de Rothschild.*)

ing of both phases of metabolism, anabolism and catabolism, *i.e.*, of all vital processes.

Every organ or structure of the body shows evidence of this slowed vital activity: The osseous system, by the stunted growth and relative shortness of all members, the saddle-nose, the deformed skull, the undeveloped teeth, etc.; the lymphatic system, by the adenoid vegetations, the so-called fat-pads, the subcutaneous

That it is the thyroid alone which, when deficient functionally, is responsible for these morbid phenomena is shown by the fact that the continued use of thyroid preparations causes them to disappear more or less if the treatment is begun sufficiently early, while they are apt to return if it is discontinued.

TREATMENT.—Thyroid preparations are still our mainstay in the treatment of all grades of cretinism.

The initial dosage of **thyroid** (*Thyroidum*, U. S. P.) is frequently stated as $\frac{1}{2}$ grain (0.032 Gm.) 3 times a day. In some cases, however, even this dose is capable of bringing on thyrotoxic disturbances, at the start, in a system unaccustomed to the thyroid principle. It is more prudent, therefore, to begin with $\frac{1}{8}$ grain (0.008 Gm.), observe for a few days, and then increase fairly rapidly until the proper dosage is ascertained. Furthermore, as the effects of the remedy are gradual in onset and persistent, it seems unnecessary to give more than 1 dose a day. Kendall's **thyroxin** (*Thyroxinum*, U. S. P.) is also available, and is administered in doses of 0.2 to 1.0 milligram ($\frac{1}{325}$ to $\frac{1}{65}$ grain).

An important feature to be borne in mind in the treatment of these cases, however, is that while some patients soon improve under very small doses, others require relatively large doses to progress satisfactorily. The doses may be enlarged very gradually and the use of thyroid stopped for a week if any untoward phenomenon appears. Insomnia, restlessness, tachycardia, wasting, sweating and exhaustion may ensue if the dosage be excessive. Screaming due to pains in the joints, simulating rheumatic arthritis, and even convulsions resembling those of epilepsy, may be produced, due to the excessive catabolism, entailing an accumulation of toxic wastes in the blood. All the untoward effects cease, however, soon after the administration of the thyroid ceases, and, if its use is resumed a week later in smaller doses, they are not apt to recur.

Another phase of the treatment which requires special watching is the production of deformities of the legs,

such as genu valgum or varum, if the child is allowed to walk too soon. As these deformities are also due in part to a deficient intake of calcium to meet the needs of the bones in calcium phosphate, **lime water** added to the child's milk, or **calcium lactate**, contributes materially toward their prevention. If the child be very short in stature, **lecithin** in 2 grain (0.13 Gm.) doses three times a day will markedly promote growth.

ADIPOSOGENITAL DYSTROPHY.

SYNONYMS.—*Fröhlich's disease*; *dystrophia adiposogenitalis*; *adipositas cerebialis*.

DEFINITION.—A form of obesity in which the genital organs remain more or less undeveloped, due to inability of the great basal ganglia, as a result of lesions or pressure upon the latter or upon the pituitary body, to transmit sufficiently active impulses to the various endocrins, the thyroid and adrenals in particular, thus reducing below normal both thermogenesis and metabolism in all tissues, including the gonads. (Author's definition.)

SYMPTOMS.—Adiposogenital dystrophy being due, although in rare instances only, to tumor of the pituitary or in neighboring tissues, headache may occur as an early symptom. It is located, as a rule, in the frontal or temporal regions, or behind the eyeballs, which, in turn, feel as if distended. It may last from an hour to several days, and is apt to be brought on by any condition capable of causing cerebral congestion, excitement, mental strain, indiscretion in diet, etc. Visual disturbances of various kinds may then be noted, affecting first, as

a rule, the color fields, and ranging from temporal hemianopsia to amaurosis. Strabismus, internal or external, may also be caused by pressure of a neoplasm upon a cranial nerve. In the vast majority of cases of true adiposogenital dystrophy, however, there is no tumor nor any abnormal tendency to headache.

The appearance of the patient is characteristic. The more or less marked obesity causes the face to be round and moon-like. The patient may be short, growth having been arrested in childhood, as in the juvenile form, or of average height or even tall when adolescence is reached. Several of my cases have been of the latter type.

The obesity in males is apt to be more evenly distributed than in females, but it presents the curious feature of giving the male body the appearance of that of the female—large breasts, hips and mons veneris, and close approximation of the knees, *i.e.*, genu valgum. The abdomen protrudes abnormally, and there are large pads of fat, disposed crosswise on each side, the back, or above the abdomen, at the symphysis pubis, and to a less extent involving the buttocks. The skin is strikingly devoid of hair, notably about the genitalia and axillæ, that of the scalp being, however, virtually normal.

Even in some of the male patients, furthermore, the feminine structural proclivity asserts itself, the pelvic hair being present and distributed as it is in the female, ceasing horizontally above the pubis. The genital organs also bespeak arrested development of the secondary sex characters. The penis is rudimentary, sometimes hardly discernible, the scrotum being

also small, drawn up or buried in the surrounding fat. The testes, if present, are undescended in most cases, and, if descended to any extent, insignificant, or at least very small. The voice usually remains juvenile.

In the female sex the distribution of fat is characteristic. While general—one of my patients, a girl of 19 years, weighing, for example, over 260 pounds,—the deposition of fat occurs especially about the hips and thighs (hence the term “girdle obesity”), with more or less distribution elsewhere, *e.g.*, over the abdomen (forming an apron over the pubis in some instances), the back—which often shows the fat pads referred to above,—the breasts, calves, etc.

These disfiguring changes are apt to appear after puberty, and autopsies have repeatedly shown that the heart, liver, mesentery, omentum, retroperitoneal space, and other tissues are similarly overburdened with fat. The obesity may be relatively enormous; in a personal case, a girl of 14 years weighed 254 pounds stripped, the fat, however, being more evenly distributed than in older subjects.

The skin, as a rule, is fine and delicate, the cheeks often rosy, even in some patients beyond adolescence. It is smooth and cool in some, but in others the hallmarks of deficient thyroid activity are plainly evident, the skin being then rough, furfuraceous or scaly—the identical epiderm observed in myxedema. Although the crescents at the bases of the nails are sometimes absent, the nails themselves are usually normal. In both male and female subjects the skeleton is feminine in type, with small hands and tapering fingers, small feet, and broad pelvis. In the sexual sphere frigidity is

usual in both sexes, amenorrhea and sterility being the rule in females, especially where sexual dystrophy results in an infantile uterus. Polyuria, sometimes reaching the proportions of a true diabetes insipidus, with the attending polydipsia, are occasionally observed. Enuresis is not uncommon.

The nervous phenomena are variable, but in true adiposogenital dystrophy, in which the symptoms due to the effects of a tumor on the tissues about the pituitary body do not complicate the case, they are not apt to be of a severe nature. Irritability, deficient self-control, or conversely, languor, may be observed, but as a rule juvenile cases are good-natured and childish in their tastes and ability to acquire knowledge. This, however, presents some curious questions; in a personal case in a girl of seventeen, a grammar school education was quite within the patient's reach, excepting in one respect: arithmetic. She is quite unable to tell how much twice $6\frac{1}{2}$ makes, for example, despite the utmost desire and effort to do so. In several of my cases, on the other hand, now young adults, the intelligence is quite normal.

Auras, with attacks of petit mal or even true epilepsy, are occasionally observed. These have been attributed to pressure of a causal growth upon the uncinate gyrus or other neighboring structures. They may occur, however, without any such factor, merely owing to the slowed metabolism the disease entails and the accumulation of toxic wastes in the blood through inadequacy of the catabolic phase of the process.

The laboratory findings point distinctly to functional depression in various organs. The blood-pressure

is low—often below 100, systolic,—indicating cardiovascular inefficiency. The basal metabolic rate is also lowered, often to -30 ; this points to insufficiency of the adrenals (both cortical and medullary portions), the active factors in thermogenesis, and to a similar condition of the activator of the thermogenic process, the thyro-parathyroid apparatus. The temperature is subnormal, the oxygen intake reduced, and the CO_2 output likewise. The carbohydrate or sugar tolerance is increased; this indicates reduced hydrolysis of sugars through pancreatic insufficiency, and accounts for the presence of glycosuria in some cases.

The body presents, as a rule, a rather low hemoglobin percentage and a slightly reduced erythrocyte count. The leucocyte count and other features of the blood picture are too variable to afford any diagnostic aid.

Case of adiposogenital dystrophy in a small boy in which the X-rays revealed enlargement of the sella turcica with enlarged posterior clinoid process. Although the Wassermann reaction was negative in the patient, it was markedly positive in the father. Babonneix (Paris méd., Dec. 26, 1925).

ETIOLOGY AND PATHOLOGY.

—To understand the manner in which various factors may cause adiposogenital dystrophy, without indulging in pure assumptions as has been generally the case, the modern interpretation of the functions of the pituitary body is necessary.

We have seen that the prevailing idea that the pituitary is the source of an internal secretion has been eliminated by modern research. So decisive has this evidence been that in the last edition of his work on "Internal Secretions," Swale Vincent, Prof. of

Physiology in the London University, emphasizes the need of "a reconsideration of our whole attitude in relation to the pituitary body." Indeed, while various factors, tumors, trauma, etc., of the hypophysis may cause the adiposogenital syndrome, no lesion of this structure need be present at all. Thus, Camus and Roussy, Bailey and Bremer—the latter working in Cushing's laboratory—and others have found that even slight lesions of the basal tissues, especially if seated in the *tuber cinereum*, *overlying the hypophysis*, could cause rapid obesity and, in the young, the adiposogenital syndrome.

Again, the majority of cases of the adiposogenital syndrome show no clearly defined changes in the hypophysis under Roentgen-ray examinations or at autopsy. Histological changes in the pituitary system and its basal ganglia, lesions in the basal tissues, the pressure induced upon them from above as in tumors of the third ventricle or as in a case of hydrocephalus observed by Babonneix and Denoyelle, which they attribute, in fact, to "irritation of the tubero-infundibular region"—these are the dominant pathogenic factors in most cases.

Case with arrested sexual development, obesity, headache, vomiting and loss of vision in a boy of 17 years. At 26, the autopsy showed a papillary epithelioma of the third ventricle filling the cavity. The pituitary and all other endocrins were found perfectly normal. Lereboullet, Mouzon and Cathala (Rev. neurol., xxviii, 154, 1922).

Much has been made of the effects of feeding pituitary gland substance and grafting, but neither line of evidence can bear unbiased scrutiny. The earlier experiments of Oliver and

Schaefer (1895) showed that the hypophysis contained a substance which raised the blood-pressure. Howell, in 1898, attributed this effect and the slowing of the heart which the extract induced to the presence in the latter and in the posterior lobe of adrenin. Indeed, as since observed by Wiesel (1905), the posterior lobe of the hypophysis gives the chromaphil reaction. These cardiovascular effects are purely pharmacologic and in no way represent the function of the organ. Again, the posterior lobe, as a neural organ, contains the same lipoids and oxidase (adrenoxidase) as all other nervous structures, in the form, so to say, of a concentrated extract of the adrenal cortex, as represented by lecithin and cholesterol embodied in its neural elements, and adrenalin, the agent which causes this lobe to give the chromaphil reaction.

As regards the rôle of the anterior lobe in the pathogenic process, the evidence adduced by Goetsch, that feeding of this lobe increased the weight while hastening growth and the development of the gonads in young rats, demonstrates in no way that as such it is able to counteract the obesity of adiposogenital dystrophy. To increase weight is not an indication that such is the case. In non-hypophyseal obesity, in fact, anterior pituitary given orally, as observed by myself in several cases, increases occasionally the deposition of fat. Pure lecithin has also in my hands produced considerable obesity, and a personal study of Robertson's tethelin showed clearly that it was to the presence of this phospholipoid in the anterior lobe that any growth effects he observed were due—effects purely of a pharmacologic order.

Indeed, none of the effects produced by these agents, tethelin or lecithin, can rightfully be regarded as due to a secretion of the anterior lobe. The pituitary extracts are mere counterparts of agents found elsewhere in the body in all tissue cells, in fact, and originally derived from the adrenals (the cortex as to the lipoids) and carried to all cells of the body at large by the red corpuscles. An additional illustration of the fact that the influence of the pituitary body is not due to a special secretion is shown by the effects of removal of the testicles, and the obesity of eunuchs and Skopzen, *viz.*, accumulation of fat in the mammae, nates, abdomen and hips, in particular. Here the absence of the testicular interstitial cells so reduces the supply of lecithin—of which these cells are mainly composed—to the tissue cells of the body at large, that *thermogenesis*, to which lipase owes its fat-reducing activity, cannot be carried out, the end-result being obesity.

Deficient activity of the pituitary, whether as a result of removal, partial or complete, tumors, cicatricial lesions, pressure, or any other inhibitory process, produces obesity by a similar inhibition of thermogenesis and through it a corresponding reduction of the lipolytic activity of the pancreatic lipase. We have seen elsewhere how this is produced. In 1903 I submitted ("Internal Secretions," Vol. I, p. 593) that both lobes of the pituitary body served for the elaboration of nervous energy. Briefly, the anterior pituitary receives leucocytes and red corpuscles which contain and empty therein their lecithin, cholesterol and adrenoxidase; these are collected in the *pars intermedia*, thence trans-

ferred to the posterior pituitary, where they are adjusted to the needs of the basal nuclei, which themselves are centers of nervous energy.

The pituitary body and the basal nuclei in the overlying tuber cinereum thus constitute a powerful electro-dynamic center whence all the true endocrine organs, the thyro-parathyroid system, the adrenals, the thymus, the pancreas, the spleen, and also the kidneys, receive their secretory impulses, the nervous intermediary being the sympathetic nervous system.

In the light of this interpretation it becomes easy to understand how the many different causes of adiposogenital dystrophy can evoke its dominant symptoms, obesity, hypogenitalism, etc., and in many instances, defective mental activity, without introducing into the process a so-called "internal secretion," the existence of which has never been demonstrated since Vassale and Sacchi, of Turin, suggested it in 1895. Tumors, at first thought to be the sole cause of the disease, are now known to be but rarely so. Even were it otherwise, any form of growth capable of interfering with the accumulation in the pituitary of the biochemical agents which collectively develop nervous energy for the great basal nuclei could cause the disorder by blocking more or less the impulses to the various endocrins that sustain the metabolic rate, including the catabolism of fats.

It is because the injuries or lesions produced by Camus and Roussy, Bailey and Bremer, Houssay and

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adiposogenital syndrome. Injuries, sclerotic areas following infections, lues, chronic tonsillitis, pneumonia, meningitis, etc., in the pituitary body itself or in the basal nuclei of the tuber cinereum; indeed, pressure by overlying tumors totally disconnected from the pituitary body proper, or by the third ventricle (edematous tension of hydrocephalus), suffice to provoke the disease by interfering with the flow of impulses from the great basal ganglia.

In 3 cases described by the writer the disease was associated with unusual types of tumor in the base of the brain, none of which started in or infiltrated the pituitary body. In the first 2 cases the tumor was a cystic ependymoma, and in the third case a cholesterin-containing cyst. Armstrong (Brain, June, 1922).

In a case of congenital hydrocephalus, polyuria, and the adiposogenital syndrome in a girl of 14, with the pituitary intact, the writers found the tuber cinereum compressed and flattened by the intraventricular tension. The nuclei of the tuber region showed grave cellular lesions. Urechia and Elekes (Revue neurol., Mar., 1925).

In a case of adiposogenital dystrophy, chronic encephalitis of the base of the midbrain (tuber, infundibulum, corpora mammillaria and substantia perforata) was found by the writer at autopsy. The pituitary was almost normal. Kraus (Med. Klinik, Mar. 26, 1926).

On the whole, all the etiological factors do precisely what the laboratory lesions did: They interfere with free arrival of secretory impulses to the adrenals, thyroid, parathyroid, thymus and pancreas, and by slowing metabolic rate, prevent the development of the gonads (which is censurate with function of the adrenal cortex) activities, in-

cluding the physiological consumption of tissue fats.

TREATMENT.—My own experience in the treatment of these cases soon led me to realize that benefit was seldom obtained from organotherapy, anterior or posterior pituitary, ovarian gland, or testicular or orchic extract, or any combination of them, if **thyroid gland** was omitted. This gland alone, when a good active preparation was used, sufficed to turn the tide and in some instances, where, for instance, the testes were undiscernible in the scrotum, even up to the fourteenth year, to cause their development in from 6 to 12 months. Nor need the dose be large in such children; $\frac{1}{2}$ grain (0.03 Gm.) three times a day, after meals, is sufficient. In keeping with my interpretation of the functions of the thyroid apparatus, the thyroid administered awakens the thermogenic activity of the tissue lecithins—of which the interstitial cells of both the testes and ovaries are mainly composed, and with which all fats are closely connected,—and the adiposogenital dystrophy soon begins to show its remedial effects. Rarely, larger doses are needed. In adults, 1 grain (0.065 Gm.) thrice daily is the maximum dosage used.

The other glands may be used with advantage, but not empirically, for they have their special indications. In the girdle type of obesity of women, for instance, the hips, buttocks and waist may attain very large size. In such cases the sympathetic system is unable to maintain the circulatory equilibrium, and **anterior pituitary**, containing, as we have seen, all the constituents of nerve tissue—lecithin, cholesterol and adrenoxidase,—is eminently suited to do what it actually

does, *viz.*, redistribute the fat to the normal relative proportion each tissue should contain, and in children, promote growth.

Case in a girl of 12 years who had begun to develop adiposogenital dystrophy at 7 and when seen resembled a fat woman at the menopause. Under prolonged treatment alternately with **anterior and posterior pituitary tablets** and **fresh substance** she gained over 12 centimeters in height in 1 year and lost weight. De Quervain (Schweiz. med. Woch., July 15, 1920).

Case of an infant who, in the third month, became stout, sleepy, stupid, and polyuric. **Thyroid gland**, $\frac{1}{4}$ grain (0.015 Gm.) *t. i. d.*, overcame the polyuria, tongue protrusion, and dribbling of saliva. **Whole pituitary gland** was added and increased up to 9 grains (0.58 Gm.) a day, with thyroid up to 3 grains (0.2 Gm.) a day, with resulting decrease of somnolence and brightened mental condition. Kay (Endocrinology, May, 1921).

When, as in some children or adolescents, more or less mental deficiency or amentia exists, the anterior pituitary, used as above, proves helpful because of the lecithin it contains; but in them it is well to add **lecithin**, 1 to 2 grains (0.065 to 0.13 Gm.) in chocolate tablets after each meal. The mental efficiency of the child soon shows signs of improvement.

Adjunct measures, such as **massage**, life in the **open air**, **exercise** and companionship calculated to develop the child's mental equipment, are of great aid. **Light X-ray dosage** to enhance pituitary activity has been advocated.

Using *small* doses of **X-rays** with the intention of **promoting** pituitary function, the writers obtained satisfactory results. Four exposures were given at 4-week intervals. In addition, **pituitary and testicular extracts** were administered. Ascoli (med., July 10, 1920).

Case of a woman of 21 whose weight rose in a few years to 115 kilograms (253 lbs.). She was then reduced to 68 kilos. (150 lbs.), but became totally blind. The X-rays showed sellar enlargement. By **X-ray treatment** for 10 days only she was enabled to distinguish light from darkness. Upon further protracted and vigorous X-ray treatment the tumor seemed to be destroyed, vision being soon restored to one-half normal and facial paralysis being cured. The writer advocates trial of the X-rays before resorting to **operation** in such cases. Ranschburg (Deut. med. Woch., Oct. 27, 1921).

All cases should, of course, be examined with great care. X-ray examination of the skull to determine the condition of the sella turcica and thereby some possible disorder of the pituitary; urinalysis, blood analysis, with differential count, and finally, basal metabolism tests, are eminently required in all such cases. The Wassermann reaction is not to be depended upon in children, as parental lues may be the original cause.

The obesity for which endocrine glands can be incriminated is usually a partial, regional, not a diffuse, uniform obesity. While in ordinary obesity **dieting** and **physiotherapy** are the main reliance, in endocrine obesity the gland or glands involved must be investigated, and the possibility of **surgical treatment** and **radiotherapy** considered, tentative treatment for syphilis applied, together with organotherapy. In the writer's experience, **pituitary** or **suprarenal extract** seemed to increase the efficacy of **thyroid** treatment. Lereboullet (Paris méd., May 6, 1922).

Adiposogenital dystrophy seems to be always a pluriglandular affection. In the case reported a severe infectious disease at the age of 8 (severe headache predominating in the clinical picture).

normal in every respect. Implantation of a testicle from another man (undescended testicle) at the age of 22 had failed to modify the condition in any way during the 8 months to date. N. Schereschewsky (*Revue franç. d'endocrin.*, iii, 395, 1925).

The headaches are best treated by means of **acetylsalicylic acid** or **acetphenetidin** in 5 grain (0.3 Gm.) tablets, while the presence of a pituitary tumor may necessitate a **decompression operation**.

INFANTILISM.

Various types of endocrin infantilism have been attributed to the pituitary body alone, even though they present a different symptomatology. The varying phenomena observed, however, are in most instances due to the fact that not all endocrin glands governed by the pituitary are equally active. When there is perfect parallelism in their functional activity, weakened impulses from the pituitary will correspondingly inhibit the secretory activity of all the glands and prevent growth uniformly. In a child this will result in the Lorain type of infantilism, a diminutive individual, as we shall see, but one preserving the conformation of a normal child, of which he is, so to say, a reproduction in miniature. That such cases are due primarily to pituitary debility is shown by the fact they may be caused by lesions of a destructive type of the anterior lobe, which, we have seen, is the collector, so to say, of the materials out of which the nervous energy in the posterior lobe and the great basal ganglia is elaborated. The latter are functionally impaired, together with all the endocrin glands and the circulatory mechanism, and tissue meta-

bolism is slowed in proportion, the child's development and growth being arrested long before puberty.

This perfect, though slowed, functional equipoise does not, however, prevail in all subjects; it is, in fact, comparatively rare. In some, involving the adrenals, for instance, local hemorrhages caused by one of the infantile infections, notably diphtheria, may have so impaired the cortex of these organs as to inhibit not only the development of secondary sex characters and hair growth, but also the whole systemic thermogenic mechanism, through deficient formation of the lipoids, both lecithin and cholesterol, which the cortex elaborates from food. If, analogously, the adrenal medulla is the seat of lesions, oxidation is inadequate. We no longer have merely a *quasi*-perfect little man of the miniature type, but a form of infantilism that is known by the French as *nanisme cardiaque*, in which there is delay and impairment of all nutritional processes with dwarfism as result.

Similar sclerotic lesions in the thyroid apparatus may contribute a cretinoid or myxedematous touch to the infantilism present, with its dry skin, coarse hair, saddle nose, etc.

This will suffice to emphasize the fact that "infantilism" cannot be regarded as a uniform condition in which a single line of treatment will bring satisfactory results. Yet, at the present writing (1927), the subject of infantilism, which means, as first defined by Lasègue, who introduced the term, "retarded or arrested development of the body and mind with persistence of infantile characteristics," is in a state of bewildering confusion due to efforts in the opposite direction,

i.e., the erection of a multiplicity of types, and to the prevailing obscurity concerning the functions of the various organs involved. In the light of the functions I have attributed to the endocrin organs, however, it becomes possible to explain the pathogenesis and symptomatology of the clearly defined forms of infantilism, and to outline, at least, rational remedial measures where such can be applied.

Cretinism, Mongolism and adiposogenital dystrophy are in reality forms of infantilism, if we accept the definition of Lasèque. They represent the effects of deficiency of the thyroid, adrenals (cortex) and pituitary. Yet, special types of these have been recognized.

Myxinfantilism, or the infantilism of Brissaud.—This may be regarded as cretinism (*q.v.*) in which growth is stunted very early, the proportions of the little cretin being those of an infant, with association of an aged face. The treatment of these cases is that for cretinism, but with the mother as intermediary if suckling is possible.

Hypophyseal Polyglandular Infantilism.—This is the form previously mentioned of deficient functional activity (a result itself of some early lesion—neoplasm or defect—in the pituitary or the great basal ganglia) which, by inhibiting the energy of impulses to the various endocrin organs, the adrenals, thymus and thyroid particularly, correspondingly restrains the normal growth process. Two forms of this type have been recognized:—

Juvenile Form.—This form, first described by Lorain in 1871, is constituted, as previously stated, by very small individuals of either sex in whom the conformation of the body is well preserved, with the exception, in the

majority, of relatively long lower extremities, due to late closure of the epiphyseal disks. The basal metabolism, blood-pressure and temperature are usually subnormal. The face, including the nose, and the voice are childish, but the mind may be quite normal for the patient's age, as in several of my own cases. The muscles, including those of the extremities and nates, are flat, poorly developed, and relatively weak. The pelvis is narrow in both sexes, the external genitalia being more or less rudimentary. There is also virtual absence of hair on the mons veneris, face and axillæ, even in postadolescent cases.

Adipose tissue is usually deficient, the limbs being flail-like, and the breasts, mons, and abdomen flat. All this applies as well to the internal organs, the heart remaining infantile, the vessels narrow, and the renal apparatus and the intestines, small and large, undeveloped. Glycosuria, enuresis and, particularly in tumor cases that have had to undergo decompression operations, polyuria or diabetes insipidus, are likewise observed.

Analyzed, these cases clearly indicate the slowed biochemical process involved. The insufficiency of all endocrins accounts for the arrest of development; what functional activity they possess under the inadequate pituitary impulses they receive suffices to sustain metabolism, but only for the undeveloped body. The surplus anabolism required for growth is lacking, and the infantile state is perpetuated.

Adult Form.—This form, first described by Claude and Gougerot as "*insuffisance pluriglandulaire endocrinienne*"—thus indicating that polyglandular insufficiency of various endocrins

had been recognized by these authors,—occurs as a result of many disorders of an infectious and toxic nature, and in some instances has been attributed by them to congenital debility of the various endocrins. Here again, however, we find the same symptomatic trend as in the Lorain type, though progressive instead of stationary, and occurring in adults of from 25 to 30 years—after, therefore, development of the sexual organs.

Metabolism is slowed, subnormal temperature and sensitiveness to cold being salient symptoms. The pulse is slowed and the blood-pressure lowered. Mental activity is depressed, particularly when any psychic effort is prolonged. The muscular system is more or less asthenic, marked lassitude following exertion. The muscles themselves lose their firmness and rounded outline. Sexual appetite is gradually reduced and is ultimately lost, the testicles becoming withered. Menstrual disturbances and premature menopause are usual. The hair loses its luster, then begins to fall, the facial hair, eyebrows, etc., doing likewise. Even the voice becomes high-pitched when the disorder occurs in adolescents, thus emulating the preceding type. Polyuria or diabetes insipidus is commonly observed.

The biochemical process here is the same as in the juvenile form, but the functional parallelism of the various endocrins of the latter no longer prevails. Stigmata indicating progressive degeneration of certain glands sooner or later assert themselves.

Insufficiency of the adrenals is indicated by the yellowish brown—Addisonian-like—hue of the skin, the progressive myasthenia, and the gastrointestinal disorders, the latter be-

ing due to relaxation of the gastrointestinal muscularis. Thyroid failure may likewise occur, as shown by myxedematous areas especially about the face, and increasing dryness and scaliness. The parathyroids also indicate their impaired functional efficiency by the occurrence, in some cases, of spastic muscular contractions, and occasionally, of true tetany.

The trend of events likewise points to a progressive degeneration of the whole endocrin system. While remissions sometimes occur, cachectic phenomena, all emphasizing endocrin failure, gradually supervene, ending in death after several years, unless, as is frequently the case, owing to the weakening of the defensive functions, in which, we have seen, the endocrins take an important part, an intercurrent disease closes the scene earlier.

Sexual Infantilism of Adults.—This disorder, first described by Gandy in 1906 and termed by Brissaud and Bauer in 1907 “adult or tardy infantilism,” illustrates clearly the polyglandular effects of lesions of the hypophysis. The need of introducing “sexual” into its designation, as in the above heading, is emphasized by the fact that its essential feature is the loss of sexual characters in adults—usually between the twentieth and fortieth years. Its polyglandular nature had been advocated by Rénon, Claude and other French observers, while Gandy and others attributed it to hypothyroidism. Analysis of the question as a whole, however, shows that Rénon’s conception was justified, *i.e.*, that we are dealing with a polyglandular syndrome, even though he was not familiar with the neural connection between the pituitary, basal areas, and the various endocrins involved.

The lesions found post mortem were situated in the tuber cinereum, the region of the basal ganglia, and were syphilitic, *i.e.*, gummas or sclerotic areas in the soft tissues; or, again, consisted of osteoperiostitis of the clinoid processes themselves or of the sellar floor (Gandy). Hence the early persistent headache and the occasional occurrence of acromegalic phenomena (Dalché) due to the primary stimulation by the pituitary disorder. When the luetic lesions are sufficiently advanced to impair the conductivity of the nerve paths to the adrenals, the characteristic effects of insufficiency of the latter appear, *viz.*, hypothermia, frilosity, reduced vascular tension, sweating, somnolence, physical and mental torpor, and polyuria due to relaxation of the renal arterioles—all benefited materially by the therapeutic use of adrenal substance. Phenomena traceable to hypothyroidia also become manifest in the form of a myxedematous, waxy pallor and puffiness of the face, dryness and scalliness of the skin, loss of hair, including the eyebrows, and hoarseness, with thyroid atrophy as a practically invariable finding.

Subnutritional Infantilism.—Under this title may be grouped those forms in which disorders of the alimentary tract prevent the assimilation of sufficient food products to enable the endocrins to carry on metabolism and sustain body growth. A large number of examples of this form of infantilism occurred during and following the World War. The same cause underlies the presence of many such cases in the slums of great cities.

What is generally known as *Herter's infantilism* (1909) belongs, from my viewpoint, to this type, although Herter

himself attributed it—rightly as primary cause—to toxins of bacilli resembling Tissier's *Bacillus bifidus* and another which he styled the "*Bacillus infantilis*." While the initial factor is probably bacterial, as suggested by the early clinical history, the very pale gray, bulky, sour and very foul stools, consisting mainly of non-hydrolyzed fats, and the indigestion and emaciation, all recurring at intervals, evidences of general biochemical impairment then appear, graver relapses being attended by the addition to the morbid stools of calcium and magnesium in excess and of unsplit carbohydrates and proteins. Arrest of growth and development then becomes manifest, the child becoming puny and asthenic, with its stature and weight several years behind those of normal children of the same age. That the pathogenic factor of this form of infantilism is subnutrition, the body failing to receive, owing to the gastrointestinal disorder, its vital pabula in adequate quantities, seems obvious.

The writer adopts the American point of view on digestive infantilism. He agrees with Herter that the disturbance may be due to chronic toxoinfections of the intestine during the child's second year. Comby (*Arch. de méd. des enfants*, Sept., 1924).

Three children observed with the Herter picture of intestinal infantilism who developed rickets late, long preceded by osteoporosis. The tendency to rickets had probably existed from the first, but had been masked by the undernourishment and the arrest of growth from the metabolic derangement. F. Lehmann (*Monats. f. Kinderheilk.*, May, 1925).

The process through which growth is stunted in these cases brings in the endocrin organs to a marked de-

gree. The pabula assimilated in insufficient quantities include those out of which the adrenal products, both cortical—lecithin and cholesterol—and medullary—adenoxidase or adrenalin,—are elaborated, thus striking at the very roots of thermogenesis, the foundation of all vital activities. Hence the marked sensitiveness to cold, the frequent subnormal temperature, the cold hands and feet, the cyanotic appearance of the face, lips and nails, and the myasthenia.

That the pituitary is itself the victim of the subnutritional process and, therefore, aggravates the morbid trend by its inability to activate sufficiently the whole endocrin system seems clear, thus imposing upon the victim a vicious circle in which subnutrition is the fundamental factor.

Pancreatic Infantilism.—This form, first described by Byrom Bramwell in 1902, is in a measure closely related to the form just described, but can only be accounted for by taking into account my interpretation of the function of trypsin in the process. We have seen that this pancreatic enzyme is that which carries on cellular activities in all tissue cells, and that its proteolytic activity is efficient in proportion as the heat energy liberated by the interaction of the oxidizing agent and lecithin is great. A deficient production of trypsin in a child, therefore, means deficient growth and development.

In Bramwell's case the only symptom, aside from the arrested bodily and sexual development, was chronic diarrhea with flatulent distention of the abdomen. Pancreatic extract alone corrected both conditions. Before its use the patient had not grown at all for eight years. The develop-

ment began soon after the pancreatic extract was begun, 10 $\frac{7}{8}$ inches being added to his height and 47 $\frac{1}{2}$ pounds to his weight. The infantile aspect and voice disappeared, while the sexual development became normal. Similar cases have been reported by others.

In a case of pancreatic infantilism observed by Ransom, but seen too late to permit of treatment, the autopsy showed as dominant lesions considerable fibroid thickening of the smaller pancreatic ducts with partial atrophy of the acini. In Bullrich's case, however, though it was seemingly one of pure pancreatic insufficiency, necropsy showed that various endocrins were involved even more than the pancreas itself.

Renal Infantilism.—This form, which usually includes dwarfism and at times bone deformities, is but another type of polyglandular infantilism in which interstitial nephritis is the outstanding disorder. We have seen (Volume IV) that diabetes insipidus is clearly traceable, as I pointed out two decades ago, to pituitarobasal deficiency, which, owing to correspondingly weakened impulses, results in relaxation of the renal arterioles. Prolonged, this condition often entails nephritis, the onset of which in these cases is known to be insidious.

Simultaneously, however, other manifestations of polyglandular insufficiency appear. Although the bone deformities may begin during infancy or nearer puberty, some patients only show dwarfism; but in all the osteogenic process is evidently at fault, as indicated by genu valgum, liability to fractures, ricket-like beading of the ribs, and infantile development of the long bones, with areas of

irregular calcification due to deficient calcium metabolism. The bony trabeculae have been found replaced by fibrous tissue trabeculae, especially near the epiphyses. At times the bone deformities develop rapidly, genu valgum, for instance, occurring within a few weeks.

The pathogenic process is clearly traceable to the adrenal cortex and thymus, both of which supply the bulk of the phospholipoids that take part in the upbuilding of bone, while the parathyroids influence calcium metabolism, the thyroid secretion acting as activator. Unused phospholipoids are partly eliminated as phosphoric acid, and, the renal vasodilation aiding, a chronic form of interstitial nephritis is provoked, the dominant symptoms of which are clearly defined, along with the diminutive size and rachitic appearance of the patient.

Precocious Senility and Infantilism.

—In this condition, termed “progeria” by Gilford, the growth of a child is delayed or arrested, and senility or senile decay is so rapid that in some, a child of a few years may present the appearance of an elderly person. In Rand’s case the child resembled a woman of seventy-five years. The skin was soft, loose and elastic, and showed many wrinkles, the face being fair but freckled. The subcutaneous tissue over the entire body was atrophied, the breasts being of the senile type. The skin showed large superficial veins and cyanosis about the inner canthi, while the arteries were very tortuous. Although the heart was not enlarged, the sounds were loud. The child tired easily. While no true signs of rickets were present, there was congenital disloca-

tion of the hips, waddling gait, marked dorsal kyphosis, and flat foot due to laxity of the tarsal muscles. The hair of the head was very abundant and very dark, but the rest of the body was entirely devoid of it. The eyes were straight; the ears were large. The Binet-Simon test showed her mentality to be that of a child of but one year her junior, even this being accounted for by deprivation of all schooling. The thyroid was not enlarged, but the sella turcica appeared small radiographically. The peduncular region and pineal gland gave no abnormal shadows.

In a case of Gilford’s, a sister suffered from rickets. The patient, a boy, began to lose flesh at 6 months. The nails shrivelled and the hair began to fall out, leading eventually to alopecia universalis. At seven there was marked myasthenia and dyspnea sufficient at times to threaten suffocation, especially at night. At 14 the boy was but 104 centimeters (41 inches) tall—the size of a child of 5 years—and presented the appearance of a wizened old man. The long bones were very thin, and the teeth few, several being carious. Two years later, he had grown slightly, but died of asphyxia. At the autopsy, the thymus was persistent and greatly enlarged, but fibrous. The mitral valve was atheromatous, the aorta and coronaries being calcareous.

Most of the main endocrins have in turn been incriminated as the seat of the primary morbid processes, but in the light of my labors it is probable that all the glands concerned with general metabolism take part in the pathogenesis of this disorder, the adrenals in particular. Destructive lesions of the pituitary have also been

found, while the thymus has been observed to be sclerotic.

On the whole, progeria appears to be due to deficiency of the materials, notably the phospholipoid, which the thymus serves to supply during the process of growth and development, including those materials that endow the pituitary with its rôle—that of supplying pabula out of which the great basal ganglia create their nervous energy.

Encephalic Infantilism.—A prolific source of confusion when the identity of a case of infantilism is to be established is that brain lesions may also act as underlying causes of defective or arrested development. Prominent among these are the general paralyses of children resulting from disorders initiated when the cerebrum and its commissural and projection fibers are not entirely formed; encephalitis, intra- or extra-uterine, leading to cerebral sclerosis, porencephaly, atrophy, etc.; also Little's disease, in which premature labor sets in before complete development of the pyramidal tracts has occurred. As the myelin of nerves is formed only during the first months of infancy, the inadequate development interferes more or less with the structural formation of these important paths, atrophy extending down the spinal cord being the ultimate result.

TREATMENT.—The treatment of infantilism necessarily requires, as indicated by the foregoing divisions of the subject, a clear identification of the type in hand.

In *myxinfantilism*, that of *Brissaud*, we are dealing with cretinism, but with the dwarfism unusually marked. While, as stated, the treatment indicated for cretinism (*q.v.*) is that of

choice, with **thyroid** as the dominant remedial agent, the low stature betokens the need of **lecithin** or **defatted thymus** in addition, to promote the formation of calcium phosphate. In some, **lime water** or **calcium lactate** is required to promote the bone-forming process. In breast-fed infants, these measures should likewise be resorted to, but through the intermediary of the mother.

Case of infantilism in a girl, aged 7, whose aspect and mentality were those of a child of 3. Under treatment with **thyroid extract** she began to improve immeasurably almost at once. Oswald (*Schweizer med. Woch.*, Aug. 7, 1926).

In *hypophyseal polyglandular infantilism*, the *juvenile* or *Lorain type*, the uniform distribution of the subnormal activities means, as the title suggests, subnormal activity of the pituitary and basal ganglia. As this involves a deficient liberation of nervous energy to all the endocrin glands, while **lecithin** is the systemic growth agent, **lecithin** pushed to its physiological limit is indicated as fundamental thermogenic factor, while **suprarenal gland** in 2 grain (0.13 Gm.) doses will increase the oxygen intake. To activate the process, **thyroid gland** should also be given, though in small doses, not more than $\frac{1}{4}$ grain (0.016 Gm.) twice daily, as larger doses, by causing exaggerated catabolism, would tend to offset the beneficial effects.

Cases in which a tumor or destructive lesion seriously impairs the structure of the pituitary body seem to resist treatment, a fact suggesting that the latter only raises to greater efficiency the inadequately active organ.

Three cases of the Lorain type of infantilism observed in males, 19, 22 and 25 years of age, who, though perfectly proportioned, showed mental enfeeblement and suffered from peri-

odical convulsions. X-ray examination showed in 1 case almost complete absorption of the clinoid processes, with a shallow sella turcica and an extensive calcareous growth; in the second case, the sella was normal. The use of **anterior lobe** in all proved useless. Webster (Jour. Roy. Army Med. Corps, xxxix, 59, 1922).

In the *adult form*, the indications are very similar, although the purpose to be attained is different, *viz.*, restoration of waning thermogenic activity. **Lecithin**, the dominant thermogenic agent, is of primary importance, but greater emphasis is to be laid upon the adrenal side of the problem, and the case treated as one of Addison's disease. The posterior pituitary (**pituitarium** of the Pharmacopœia) in large doses orally, and the 1:1000 **adrenalin** solution in 10 minim (0.6 c.c.) doses three times a day, besides the lecithin, are highly beneficial in these cases.

The *sexual infantilism of adults* being due in most instances to syphilitic infection, antiluetic treatment, comprising **mercurials**, the **arsenicals** and the **iodides**, is indicated. The **biniodide of mercury** in $\frac{1}{16}$ grain (0.004 Gm.) doses three times daily may be safely used in these cases even when non-luetic, as mercurials are powerful stimulants of the entire endocrin system. **Lecithin** is likewise of advantage in these patients to restore the systemic thermogenesis; it should be used at intervals of one month, ceasing meanwhile the administration of mercurials, which are to be resumed when the month is up. Where polyuria is present, **posterior pituitary** in $\frac{1}{10}$ to $\frac{1}{2}$ grain (0.006 to 0.03 Gm.) doses should also be given, but continuously to promote constriction of the renal arterioles.

In *subnutritional infantilism*, the treatment depends upon the stage during which the patient is seen. If the condition is met with in a child during the Herter period of primary intestinal disorder, the nature of the intestinal flora present should be determined and the treatment adjusted to it. Restriction of fats and carbohydrates has been advocated in these cases, mainly because of their inadequate absorption, but the defect is primarily due to the child's inability to hydrolyze these foods. The aim, therefore, should be to restore this function. This may be done by administering **holadin** (Fairchild), an active combination of pancreatic enzymes, in 1 to 3 grain (0.065 to 0.2 Gm.) doses, according to the age of the child, after each meal. Minute doses of **calomel** ($\frac{1}{24}$ to $\frac{1}{12}$ grain—0.0027 to 0.0054 Gm.) have been found useful in these cases. As I have pointed out, mercurials are powerful activators of endocrin functions. In the adult type, a diet rich in fats and carbohydrates, along with **lecithin** and **codliver oil**, is promptly effective. **Sunlight** is of great therapeutic value in both the Herter and adult types of infantilism.

Case of a boy of 6 years who presented a marked cretinoid appearance with a thick, protruding tongue, etc. This condition had started after a severe acute gastroenteritis experienced in the 25th week of life. The child's development then began to be retarded. **Thyroid** and **suprarenal substance** were given in combination. In 3 months the height increased from 82 to 92 centimeters, and in subsequent years satisfactory progress was made, the child attending school. Rodenacker (Deut. Zeitsch. f. Ghir., Sept., 1921).

Pancreatic infantilism is readily met by the use of **pancreatic extracts**.

Ordinarily **pancreatin** suffices in very young children, but in older children **holadin**, given as specified above, is of greater service. As I have pointed out, pancreatic enzymes are the active factors in the life process, when activated by the heat energy liberated by the interaction of the adrenal and thyroid secretions. Hence the marked advantage of administering simultaneously **suprarenal gland** in doses of 1 to 2 grains (0.065 to 0.13 Gm.) three times a day.

Renal infantilism is in reality a form of rickets. Treatment here, however, demands primary attention to the interstitial nephritis; but the dietetic restrictions should not be such as to exclude fats, since they are prominent factors in the process through which the lipoids, including lecithin, are absorbed by the tissue cells. Hence, **milk** and **cream** should form the basis of the dietetic treatment.

When the excessive excretion of phosphoric acid and phosphates has been reduced to normal limits, the

cause of the nephritis should be eliminated. This may be done by administering **lecithin**, which, as shown by Waldemar Koch, promotes the solubility of calcium. If, simultaneously, we then administer **thyroid** in $\frac{1}{4}$ grain (0.016 Gm.) doses together with **parathyroid** in $\frac{1}{10}$ grain (0.0065 Gm.) doses twice daily, the metabolism of calcium will be restored to normal limits and distinct improvement follow. In addition, the treatment for rickets (*q.v.*), *i.e.*, **heliotherapy**, **open air life**, etc., is indicated.

In *precocious senility* or *progeria*, the obvious indications are the use of **polyglandular remedies** employed early to offset the degradation of the entire endocrin system. The dominant note being, however, insufficiency of phospholipoids of thymic and adrenal origin, **lecithin** might prove advantageous. The author never having treated such a case, however, precise indications cannot be vouchsafed.

C. E. DE M. SAJOUS,
Philadelphia.

K

KALA-AZAR.—SYNONYMS.—

Leishmaniasis; kaladukh; non-malarial remittent fever; cachectic fever; Blacktown fever; black fever; death fever; black sickness; sarkari; saheb disease; burdwan, and dum-dum fever.

DEFINITION.—A subacute or chronic specific febrile disease caused by *Leishmania donovani* and probably transmitted by the sandfly (*Phlebotomus argentipes*), and possibly by Indian bedbugs and mosquitoes (*Anopheles*).

The parasite responsible is a minute organism, one-fourth to one-eighth the size of a red blood-cell, oval in form, having two nuclei, one large and rounded, the other small, linear, and generally lying at right angles to the larger.

SYMPTOMS.—The period of incubation varies from ten days to several months. At the onset there is usually a rigor (which may be repeated daily), followed by an irregular, high fever, which shows two remissions daily. This double remission is pathognomonic of the disease (Rogers). The temperature declines after three to six weeks of the fever, marking the termination of the initial stage. In this initial stage the spleen and often the liver are swollen, painful, and tender. Slight headache may be present. The bowels are unaffected. There is little or no nausea, vomiting, or abdominal distention. The pulse is usually unchanged.

The attack may begin with a continuous fever, exhibiting 2 remissions in the 24

hours; in other cases gastro-intestinal or dysenteric symptoms mark the onset; in still other cases, the patients may gradually develop an enlarged spleen and liver, anemia, and weakness.

After the initial stage an apyretic interval occurs, which lasts several weeks, and ends in an attack of fever similar to that of the onset. Periods of pyrexia and apyrexia alternate, the spleen, and sometimes the liver, becoming enlarged. Increasing anemia is noted and is accompanied by progressive asthenia, the patient becoming emaciated and his abdomen swollen and protuberant. Hemorrhages from the nose, gums, stomach, and bowels, or beneath the skin, may appear. The patient may die of asthenia or from one of several complications, among which are septic infections (pneumonia, phthisis, pleurisy, meningitis), abdominal troubles (diarrhea, dysentery, cystitis), purpura, and cerebral or other hemorrhages.

Serum test in which 1 c.c. (16 minims) of the patient's serum is placed in a small test-tube, 1 drop of 30 per cent. commercial formaldehyde solution added, and the tube shaken. The serum from an untreated case of kala-azar at once becomes viscid, in 1 or 2 minutes whitish and opalescent, and in 3 to 20 minutes absolutely solid and opaque. L. E. Napier (Indian Jour. of Med. Res., Apr., 1922).

TREATMENT.—The prime indication is to destroy the parasite. Rogers advises giving from 60 to 90 grains (4 to 6 Gm.) of **quinine** daily until the temperature falls or becomes of a low, intermittent type, and then 20 grains (1.3 Gm.) every morning. Castellani gives 30 grains (2 Gm.) each of **quinine sulphate** and **euquinine** daily by the mouth, together with daily intramuscular injections of 15 grains (1 Gm.) of **quinine hydrochloride**, alternating with 4 grains (0.25 Gm.) of **quinine cacodylate**.

Rogers has advised the use of a **staphylococcal vaccine**. **Red bone-marrow** has been given to counteract the anemia.

As a prophylactic measure the **destruction of the bedbugs** in the infected houses has been advised by Rogers.

Intravenous injections of **antimony and potassium tartrate** or **antimony and sodium tartrate** in such doses as 2 or 3 c.c. (32 or 48 minims) of a 2 per cent. solution have proven valuable, but often are not curative.

Urea stibamine intravenously acts more rapidly than tartar emetic, sometimes cutting short the disease.

The amount of **urea stibamine** required for a complete treatment of kala-azar ranges, according to the patient's age, from 2 to 6 Gm. (30 to 90 grains). Greig and Kundu (Indian Jour. of Med. Res., Apr., 1925). W.

KAOLIN.—Kaolin (kaolinum), also known as pipe clay, porcelain clay, china clay, or fullers' earth, is a native aluminum silicate consisting principally of the pure silicate, pulverized and free from gritty particles by elutriation. It is found in large masses in the earth, resulting from the weathering action of carbon dioxide and water on feldspar or potassium aluminum silicate. It is prepared with 5 per cent. hydrochloric acid to remove any lime that may be present, and is then levigated to remove sand and other foreign matter. This purified kaolin occurs in lumps or as a soft, white powder, odorless, but having an earthy taste. It is insoluble in water and in cold dilute acids and alkalis. When moistened it darkens and acquires a clayey odor.

PREPARATIONS.—*Kaolinum*, N. F. (kaolin) $[H_2Al_2Si_2O_8 + H_2O]$.

Cataplasma kaolini, N. F. (cataplasm of kaolin). This consists of kaolin, 565 parts; boric acid, 45 parts; thymol, $\frac{1}{2}$ part; methyl salicylate, 2 parts; oil of peppermint, $\frac{1}{2}$ part, and glycerin, 387 parts.

THERAPEUTICS.—Kaolin is a reliable aseptic dusting powder for wounds and ulcers. Richter ascribes its beneficent action to the production of a leucotaxis. An emigration of leucocytes is presumed to take place from the blood-vessels toward the deposit of kaolin wherever the surface is broken, with resulting formation of "laudable pus," the leucocytes bringing out with them the microbes from the deeper tissues. This effect is brought about by the mechanical irritation caused by the minute spicula of kaolin, which will not perforate normal

epithelium, yet wound the softer membrane of other cells.

Internally, kaolin has been used as an excipient or diluent for silver nitrate and potassium permanganate. It has been employed with good results in various gastroenteric disorders—**enteritis**, **meteorism**, **foul eructations** from the stomach, **gastric hyperacidity**, and **chronic urethritis** due to gonococci or to mixed infection. Especially impressive results have been obtained in **Asiatic cholera**. According to R. R. Walker, cholera toxin is strongly absorbed by kaolin. The more finely divided it is, *i.e.*, the more it approximates colloidal kaolin, the better the results.

Cataplasma kaolini is a useful external application in **pneumonia**, **pleurisy**, **bronchitis**, **peritonitis**, etc. It is also frequently an efficient application in superficial inflammations, **mastitis**, **orchitis**, **synovitis**, **periostitis**, **boils**, and **sprains**. It replaces and is an improvement on the old-time flaxseed and mustard poultices, stupes, liniments, and other counterirritants. Its beneficial action is due to the hygroscopic power of the contained glycerin, as well as to its heat-retaining properties and to the fact that it induces superficial hyperemia, thereby relieving the congestion and pain of **deep-seated inflammations**. Cataplasma kaolini should be applied as hot as it can be borne. By immersing the container in hot water, it may be brought to the desired temperature. It should be freely spread upon the affected surface and covered with a thick layer of absorbent cotton, retained by bandages. W.

KIDNEYS, DISEASES OF. (See also NEPHRITIS.)

ACTIVE HYPEREMIA.

SYNONYMS.—Acute congestion of the kidneys; active renal congestion.

DEFINITION.—Acute transitory engorgement of the red blood-vessels, with little or no exudation.

SYMPTOMS.—The lumbar region may be the seat of a dull pain, with accompanying slight febrile movement and acceleration of the pulse.

The urine may be scanty, or if the congestion is severe there may be complete suppression. It is dark in color, of somewhat higher specific gravity than normal, and usually contains free blood, a trace of albumin, and a few hyaline casts.

Active renal hyperemia is differentiated from acute nephritis by the small amount of albumin present, the small number and character of the casts, and the absence of edema and of uremic symptoms.

ETIOLOGY.—Active hyperemia of the kidneys may be caused by sudden exposure to cold when the body is overheated, or, more generally, to the action of irritants circulating in the blood, such as the stimulating diuretics or various other drugs (cantharides, turpentine, squill, copaiba, potassium chlorate, phenol or its preparations, and corrosive sublimate). Postoperative hyperemia is common. Unilateral hyperemia may follow nephrectomy of the kidney on the opposite side, or obstruction of the ureter of the opposite kidney by a clot, calculus, twist, or bend. Prolonged congestion induces acute nephritis.

PATHOLOGY.—On examination the kidney is found to be more or less swollen, dark red in color, and engorged with blood, which exudes freely when the kidney is opened. A cloudy swelling of the epithelia of the cortex is revealed on microscopic examination.

PROGNOSIS.—The prognosis is good if the cause is removed. Repeated attacks of hyperemia, however, induce acute nephritis.

TREATMENT.—**Absolute rest in bed** and a **bland liquid diet** are essential. **Mucilaginous drinks, water, and**

other diluents should be used freely. The securing of free action of the bowels by means of **saline laxatives**, and the use of the **hot-air bath** or **hot pack** to promote active diaphoresis, are beneficial. **Dry cups** applied over the loin and the use of **hot fomentations** are likewise valuable. **Bier's hyperemia** in its varied forms is clearly indicated in these cases.

PASSIVE HYPEREMIA.

SYNONYMS.—Chronic congestion of the kidneys; passive renal congestion.

DEFINITION.—Chronic venous engorgement of the blood-vessels of the kidneys, generally secondary in character, and due to diseases of other viscera.

SYMPTOMS.—In addition to the edema of the lower extremities due to the general venous congestion produced by the primary disease, there may be a feeling of heaviness in the loins. The urine, diminished in quantity, is dark, of rather high specific gravity, and contains a small amount of albumin, a few blood-corpuscles, hyaline casts, and epithelial cells, the quantity varying with the chronicity and the intensity of the congestion. The urine on standing may deposit urates.

Active renal hyperemia is differentiated from nephritis by the comparative absence of albumin, casts, general dropsy, and of uremic symptoms, and by the presence of a normal amount of urea.

ETIOLOGY.—Passive hyperemia is most often a feature of the general venous engorgement incident to chronic cardiac disease (mitral disease with broken compensation of the heart); chronic pulmonary disease

(emphysema, fibroid phthisis, and chronic adhesive pleurisy), or chronic hepatic disease (cirrhosis). It may also be caused by the presence of tumors, the pregnant uterus, and ascites, making pressure upon the renal veins. Nephroptosis and kyphosis may be etiologically active by their pressure effects. As rare causes we may mention thrombosis or embolism of the ascending vena cava or of the renal veins.

PATHOLOGY.—In the early stage of passive hyperemia the kidneys are enlarged, firm, and of a dark, bluish-red color. The capsule usually is not adherent. When the kidney is opened the medullary portion appears darker than the cortex and coarsely fibrous. On microscopic examination the capillaries (glomerular and medullary) are found to be somewhat dilated and their walls thickened. The epithelia may be normal, slightly cloudy and swollen, or fatty, according to the stage of the disease. There may be a slight hypertrophy of the interstitial connective tissue. In long-standing cases the kidneys are in a characteristic condition known as "cyanotic induration."

PROGNOSIS.—This is largely dependent upon the primary disease, and upon the functional activity of the heart. Chronic hyperemia may readily induce chronic nephritis with fluctuating oliguria and albuminuria, the functional cardiac activity largely influencing these latter.

TREATMENT.—The measures indicated are **rest**, a **light and easily assimilable diet**, **diuretics**, and **cardiac tonics**. As examples of these groups of remedies **digitalis** and **Basham's mixture** (liquor ferri et ammonii acetatis, U. S. P.) may be mentioned.

In the treatment of congestion of the kidney measures to restore the balance in the cardiovascular system, with restriction to a **milk diet**, or, better still, to a **salt-free diet**, supplemented by **diuretics**, according to individual indication, are important. J. M. Gesteira (Brazil Medico, Mar. 15, 1912).

EMBOLIC INFARCTS.

Anemic and hemorrhagic infarcts of the kidneys are, from a pathological standpoint, of considerable interest. Their clinical significance is slight. The "embolic, contracted kidney" is produced by cicatrices formed by these infarcts. This condition does not cause its presence to be known by symptoms except in very rare cases, when the sudden appearance of a small amount of blood in the urine, in a patient with cardiac disease associated with tenderness over the kidney and, perhaps, sudden, severe pain in the loin, may indicate a hemorrhagic infarct.

Brewer called attention to cases of severe septic type, with multiple scattered abscesses throughout the cortex, and with a clinical picture of profound sepsis, in which radical measures, *viz.*, **nephrectomy**, proved advisable.

Uric acid infarcts in the newborn are employed by the writer. They appear as yellowish-red streaks in the medullary substance, but may become the starting-point of stones in the renal pelvis. Such formation of stones occurs much oftener in boys than in girls, probably because they are heavier at birth and have a more rapid increase in metabolism, so that the water of the urine is less adequate to keep the salts in solution. Armbruster (Zeit. f. Urol., xviii, 65, 1924).

PYELITIS, PYELONEPHRITIS, AND PYONEPHROSIS.

DEFINITION.—By *pyelitis* is meant inflammation of the pelvis of

the kidney. Concomitant inflammation of the renal substance justifies the term *pyelonephritis*, and intense and extensive purulent involvement, the term *pyonephrosis*.

SYMPTOMS.—These are frequently overshadowed by those of the primary condition that causes the **pyelitis**; they are varied, also, for the same reason. The simple catarrhal pyelitis may cause slight pain and tenderness in the region of the affected kidney or kidneys, mild fever, with a turbid urine of acid reaction, showing a few pus-cells, a little mucus, rarely some red corpuscles, and perhaps a trace of albumin.

In the severer varieties, as in *calculous pyelitis*, the occasional concomitant attacks of renal colic are attended with the presence of blood and pus in the urine, with some mucus, and the transitional caudate epithelial cells from the middle layers of the mucosa of the renal pelvis. The presence of the latter, however, is not constant; hence their absence does not exclude the existence of a pyelitis, since some of the most destructive forms of the affection, as the acute or chronic suppurative or the pyelonephritic, may be unaccompanied by the presence of the pelvic epithelium in the urine. This holds true still more in the case of pyonephrosis, in which the kidney often becomes one large abscess.

In severe pyelitis the pain is very acute, coursing down the ureters. The fever is moderate, and most of the symptoms common to nephroli-thiasis are manifested.

In **pyonephrosis** and **pyelonephritis** the fever is rather hectic or typhoid in type. Paroxysms of rigors or chills, followed by a rapid rise of

temperature to 104° or 105° F. (40° to 40.5° C.), and ending in profuse and exhausting perspiration, may be observed; or, there may be marked prostration, dryness of tongue and skin, feebleness of pulse, stupor, and delirium. Pyemic cases reveal a temperature curve of irregular course, with marked remissions.

In obstructive pyelitis the urine sometimes flows freely and normally for awhile, until the increasing pain over the affected kidney ends in relief by the expulsion of the obstacle and the passage of purulent urine. This *alternation* of normal with purulent urine is indicative of a unilateral pyelitis.

The urine is *ammoniacal* in cystopyelitis. Albuminuria is shown according to the degree of pyuria and associated nephritis.

In chronic suppurative pyelitis or pyelonephritis the pyuria is variable, both in quantity and constancy. Intermittent pyuria may be due to the temporary blocking of the ureter by a stone (obstructive pyelitis). The pus is seldom mixed with epithelium in chronic purulent pyelitis. The associated intermittent fever may be like that of tuberculous pyelitis, and marked prostration, anemia, and emaciation are concomitants. Evidences of amyloid change may be revealed in long-standing chronic cases.

If, in children, urine is not obtainable, pain on pressure in the renal region is sufficient evidence for starting medicinal treatment for pyelitis. Prominent symptoms are a change in the child's disposition and an intermittent erratic temperature curve. Gerstenberger and Wahl (Ohio State Med. Jour., June, 1924).

Lumbar enlargement and fluctuation may exist in some cases of pyone-

phrosis. This may also be intermittent, being detectable while there is obstruction to the flow of pus and *vice versa*. According to A. H. Smith, at the menstrual periods pyelitis may be subject to marked exacerbations simulating renal colic.

In chronic pyelitis with progressive atrophy of the kidney uremia is likely to terminate the case.

DIAGNOSIS.—Besides excluding other affections that might be confounded with pyelitis, it is important to attend to the history of the case with a view to the discovery of the cause; the urinary findings must also be studied carefully. The very nature of this affection makes it often most difficult to exclude other affections of the urinary tract, as nephritis, cystitis, and urethritis. Any severe inflammation of the tract in which the lower portion is known to be affected is generally associated with pyelitis or pyelonephritis, from the well-known tendency to extension by continuity.

Epithelium from the pelvis of the kidney cannot well be distinguished from transitional bladder-cells; but given the indications of a pyelitis, its calculous cause is at once made clear upon the passage of the characteristic uratic or oxalatic concretions. It may happen that the urine from one kidney is prevented from flowing by the impaction of a stone in the ureter. The urine may now flow clear from the other and vicariously acting kidney until, the stone having given way, it suddenly increases in quantity and changes in character, owing to the return of the morphological elements of the pyelitis (corpuscles, desquamated epithelium, crystals, and *débris*).

Catheterization of the ureters and

renal pelves is a certain method of determining from which side the purulent urine flows. Palpation of the ureters through the vagina will sometimes reveal thickening and tenderness in cystopyelitis, and ureteral distention may sometimes be felt in pyelitis calculosa.

Vierordt mentioned having seen in some cases of pyelonephritis peculiar hyaline casts "split like a pair of trousers." Casts and albumin are usually present when the kidney-structure is involved by extension of the pyelitis, while marked pain in the region of the kidney indicates predominant pyelitis, though it does not exclude the possibility of coexisting nephritis. Marked vesical irritability points to associated cystitis; but in intense pyelitis with much pus and an acid urine, vesical tenesmus may also be troublesome. Tuberculous can be discriminated from calculous pyelitis, possibly, only by a consideration of the history and general condition, and by the detection of tubercle bacilli in the pus. The presence of a fluctuating tumor in the lumbar region is significant enough of pus, but it may be difficult to determine whether it is due to pyonephrosis or perinephric abscess; the history, pyuria, and less edematous overlying tissues of the former are important distinguishing points.

The *hemorrhagic pyelitis* of Senator, Delafield, and others, described as occurring in milder forms, and particularly in girls of neurotic types, may be revealed by the intermittent hematuria and occasional lumbar pain, lasting but a few days or a week, and followed uniformly by recovery. Digestive disturbances may be prominent in these cases.

Difficulty is sometimes experienced in diagnosing pyelitis when co-existent with cystitis—*pyelocystitis*. It should be recollected that their histories differ, pain in the lumbar region being present in the former and in the bladder in the latter; acid pus is usually characteristic of pyelitis. Importance attaches to the albumin content, which is from 2 to 3 times greater with pyelitis.

According to Rosenfeld, an alkaline reaction does not occur in uncomplicated pyelitis, while the limit of albumin in cystitis, even the severest, is 0.1 or at most 0.15 per cent.

Pottenger recommends that, with the patient sitting erect, but relaxed, the lumbar muscles be lightly palpated. If one kidney is the seat of an inflammatory process, the muscles on that side will feel firmer than normally.

Pyelonephritis and *pyonephrosis* may continue for some time without producing any symptoms. At other times acute symptoms may set in quite unexpectedly, simulating perforative peritonitis or intestinal obstruction. Usually differentiation is not difficult, however, for the symptoms in the kidney cases, instead of getting steadily worse, tend to improve after the initial acute attack. Vomiting does not recur, and there is absence of hiccup. The intestinal obstruction occurring in such cases is of reflex causation and does not long continue. M. Donati (Arch. ital. di urol., i, 112, 1924).

Report of 3 cases of *acute cystopyelitis* which had been mistaken for appendicitis or gall-bladder disease and, in 2 instances, already operated as such. The condition generally occurs in young girls or women of fair complexion, often after exposure to cold. Appendicitis or cholecystitis is simulated by the high fever and abdominal rigidity, but a distinction may be made on the basis of the lower pulse-rate, quieter breathing and less disturbed expression. In $\frac{2}{3}$ of the

due to the extension upward of a severe cystitis. Acute suppuration or interstitial inflammation of the kidney, due to metastatic or miliary abscesses, occurs as a complication of pyemia.

PROGNOSIS.—Renal complications always make the pyelitis a serious affection. Catarrhal cases recover. Calculous pyelitis tends toward chronicity. Pyelonephritis and pyonephrosis are likely to end fatally from exhaustion or uremia. Perforation and the discharge of pus into the peritoneal cavity, pleural sac, intestine, and bronchi, even, may precede death. The gravity of all cases of pyelitis depends upon the causes and upon the tendency to consecutive suppuration.

Eighteen out of 26 women with pregnancy pyelitis proceeded to term with living children; 5 others had living children born prematurely; 1 woman aborted, and 1 developed eclampsia. All recovered. These comparatively good results are ascribed to routine direct medication of the kidney pelvis, without operative measures. Weibel (Arch. f. Gynäk., Bd. c, Nu. 2, 1914).

In the pyelitis of infancy and childhood there is practically no danger to life. Under appropriate treatment recovery in a few weeks is usual, though the condition may return at intervals for many months (Wyman).

TREATMENT.—This varies according to the cause: the latter needs to be removed, its effects counteracted, and its return avoided. The treatment of calculous pyelitis is essentially that of nephrolithiasis. Primary inflammation of the lower portion of the urinary tract must be combated, causes of urinary retention and decomposition must be dimin-

ished, infectious fevers must be judiciously handled, and irritating diuretics withheld.

In all forms of pyelitis local measures are useful, in the form of **hot-water bags, fomentations, dry cupping, etc.** Internally, the use of **diluents** is to be encouraged, especially the **alkaline mineral waters, flaxseed and moss teas, barley water, lemonade, skimmed and butter milk.**

In acute cases milk should constitute the chief element in the **diet**, cereals with sugar and cream, and bread and butter making up the remainder. In chronic cases a diet similar to that appropriate in chronic nephritis should be prescribed, all **condiments, rich articles, preserved meats**, and other renal irritants being **prohibited**. **Copious water drinking** is usually to be recommended. **Alcoholic beverages must be given up.**

A complete transformation may follow suddenly on ordering a **copious intake of water** in the pyelitis of children, even when uremic symptoms are pronounced. Langstein (Med. Klinik, Sept. 14, 1913).

Among drugs selected for their soothing properties are **potassium citrate, uva ursi, and buchu.** Altering the reaction of the urine from acid to alkaline with **potassium acetate or bitartrate**, or from alkaline to acid with **sodium benzoate or salicylate**, may prove of value by providing a less favorable medium for the propagation of the bacteria present (Meara). In the event of suppuration **surgical intervention** is necessary. **Irrigation** by means of **Kelly's ureteral catheter** may be practised with good results in females suffering from purulent pyelitis. **Operation through the back** is usually

indicated in pyelonephritis and pyonephrosis. In chronic pyelitis, **phenyl salicylate**, **methenamine**, **methylene blue**, or the oils of **turpentine**, **sandalwood**, **juniper**, **copaiba**, and **erigeron** may be tried.

In the pyelitis of pregnancy **lateral decubitus on the sound side**, or the **sitting posture**, have been advocated.

Many so-called *surgical kidneys* can be saved from operation by proper **drainage** and **elimination of focal infections**. The writer obtained cures in 95 per cent. of cases, without mortality. Surgical cases included 1 each of **nephrectomy**, **nephrotomy** and **nephropexy**. W. C. Stirling, Jr. (Jour. of Urol., Jan., 1923).

Autogenous vaccines used in 19 cases of *colon bacillus pyelitis*, with cure in 6 and improvement in 5. Jervell (Norsk. Mag. f. Laeg., Feb., 1923).

In cases of pyelitis that fail to respond in 3 months to ordinary treatment, **renal lavage with colloidal silver solutions** affords a rapid, safe and practically certain cure. Four or 5 treatments usually suffice. Local anesthesia with 10 per cent. **cocaine** solution with **adrenalin** is required usually only by the beginner. The rectum should be empty. The bladder having been thoroughly irrigated with **boric acid** solution or 1:4000 **mercury oxycyanide**, 240 to 300 c.c. (8 to 10 ounces) of which are left in the bladder, and the ureteral catheter having been introduced through the cystoscope until it will go no further, 5 per cent. colloidal silver solution is injected very gently with a 10-c.c. Record syringe. Pain indicates the danger-point, and the syringe shows the capacity of the pelvis. Injections are repeated at 3 or 4 day intervals, up to 6 injections. F. A. Gill (Med. Jour. of Austral., Jan. 12, 1924).

In pyelitis in *infancy and childhood*, alkalinization of the urine for several days is curative in most cases. If **sodium bicarbonate** is not effective, alkalinity may be produced with **calcium bicarbonate**, **sodium bicarbonate** and

burned magnesia, 5 grains (0.3 Gm.) each every 2 or 3 hours. The treatment should be aided by a **vegetable diet**, favoring an alkaline urine (oranges, raisins, apples and bananas). Each passage of urine should be tested with litmus paper. If the alkaline treatment fails, **methenamine** may be given, the urine, if not acid, being acidified with **benzoic acid**, **sodium phosphate**, or **dilute hydrochloric acid**. The drug should be started in doses of but $\frac{1}{2}$ grain (0.03 Gm.) for children under 1 year, 1 grain (0.06 Gm.) for those under 3, and not over 2 grains (0.12 Gm.) for those from 3 to 5 years. Such doses may be given 3 times daily, then increased up to large amounts. Cases not thus controlled sometimes respond well to **general tonic treatment**. R. G. Freeman (Arch. of Ped., Mar., 1924).

Pyelonephritis in *pregnancy* calls for **rest** with free use of **fluids**; a **liquid diet** consisting largely of milk alkalized with **milk of magnesia**; **sodium bicarbonate** or **potassium citrate** or both, in alternation with **methenamine**, and **external heat** over the painful area. Careful attention to the bowels, to hinder multiplication of colon bacilli, is imperative. **Pelvic lavage with a silver salt** is used in refractory cases. Spontaneous abortion or premature delivery did not occur in more than 5 per cent. of the writer's cases, nor in over 5 per cent. was **interruption of pregnancy** required. J. C. Applegate (Ther. Gaz., June, 1924).

Hexylresorcinol clears up urinary infections due to the usual Gram-positive cocci promptly and completely. In *B. coli* infections, persistent treatment is usually required. It is given in enteric-coated capsules in doses of 0.33 to 1 Gm. (5 to 15 grains) 3 times daily. V. Leonard (Jour. Amer. Med. Assoc., Dec. 20, 1924).

In the treatment of *acute cystopyelitis* the writer recommends **intravenous injections** of 5 c.c. (80 minims) of a 20 per cent. solution of **hexamethylenamin** on alternate days, daily **bowel irrigations**, and **morphine** for pain. In severe cases repeated **lavage of the renal pelvis**, with or without **vaccine**

therapy, may be required. Pollitzer (Med. Klin., Dec. 21, 1924).

Neosarsphenamin commended. In adults 0.2 to 0.45 Gm. is given intramuscularly at 5 day intervals, and in children, 0.15 to 0.2 Gm. into the veins of the neck or intramuscularly. R. W. Hissem (Jour. Kas. Med. Soc., Jan., 1925).

Bovet and Huchard recommended treatment of infectious pyelonephritis by **saline hypodermoclysis**.

Surgical measures are indicated in severe purulent pyelitis, pyelonephritis, and pyonephrosis.

PERINEPHRIC ABSCESS.

SYNONYM.—Perinephritis.

DEFINITION.—Suppurative inflammation of the connective tissue enveloping the kidney.

SYMPTOMS.—The patient has a dull, throbbing pain over the kidney region that is increased by motion; when the abscess is large and presses on the large nerve-trunks, the pain shoots downward into the leg on the same side. There may be a sensation of numbness. Palpation of the region will usually elicit pain and tenderness. The patient becomes prostrated, weak, and often emaciated. Flexure of the thigh on the affected side is common. Fever of a marked remittent or intermittent type with alternating chills and profuse sweating is present, indicating suppuration. When the kidney is involved, pus is found in the urine. Later there is a localized swelling over the affected region and a gradual tumefaction of the lumbar area, progressing slowly, the skin becoming smooth, shiny, and edematous. In advanced cases fluctuation is frequently present, and if the case is tending to a favorable issue signs of "pointing" appear.

DIAGNOSIS.—The condition may be somewhat obscured by a tendency of the pus to burrow downward, as distinct local symptoms will in that case be absent. If the psoas is involved symptoms of coxitis will appear, and the pain will be referred to the knee-joint. The diagnosis is generally easy. In cases of doubt as to whether the swelling is an abscess, a hydronephrosis, or a solid mass an aseptic exploring needle will usually clear up the diagnosis.

X-rays aid in the diagnosis. In a case cited, fluid was shown. The shoulders were grasped and the patient's body moved quickly 2 or 3 times from side to side. The fluoroscopic picture showed a distinct wave. The renal region was opened and a huge sac of pus found on the renal capsule. Fussell and Pancoast (Amer. Jour. Med. Sci., Jan., 1920).

In differentiating this condition from suppurative pyelitis or from pyelonephritis we are aided by the fact that in the latter there is a diminished secretion of urine, while in the former interference with the renal secretion less often occurs. Moreover, in the latter, blood and pus are found in the urine; in the former, however, while the urine is free from blood, pus may be present, and casts are generally absent.

ETIOLOGY.—When not produced by trauma perinephritic abscess is most often a result of purulent pyelonephritis or pyonephrosis. It is, therefore, generally secondary. It may also be due to an extension of inflammation arising in the ureter or pelvis of the kidney, pelvic, appendiceal, or hepatic abscesses, spinal caries (psoas abscess), and empyema. Perinephritic abscess may complicate tuberculous processes in the kidney

and suppurating new growths, as carcinoma and cysts (including the echinococcus). As rare causes may be mentioned severe infections, as typhus fever, small-pox, and pyemia. In some cases no cause can be assigned.

PATHOLOGY.—The lax adipose tissue forming the fatty capsule in which the kidney reposes and the adjacent retroperitoneal tissue are usually the seat of the suppurative process, which usually begins posterior to the kidney. While there may be, at the start, a collection of small abscesses a single large abscess is usually found. The abscess walls are at first soft and inclined to be shreddy; later, as in the chronic cases, thick and fibrous. When the accumulation of pus is large an external bulging in the affected lumbar region may be seen. The pus has a tendency to burrow into the adjacent tissues, most frequently downward toward the iliac fossa, when it may be found pointing in the groin near Poupart's ligament. It may, however, burrow backward and discharge through the skin in the loin. More rarely the pus perforates the diaphragm and finds its way into the pleural cavity or lungs; or the abscess may rupture into the colon, vagina, bladder, or peritoneal cavity. Occasionally the pus is thin and has a very offensive odor, due to infiltrated urine. When caused by calculous pyonephrosis, calculi may be found in the abscess, having ulcerated through the walls of the kidney or its pelvis. The adjacent peritoneum often becomes thickened or hypertrophied. In rare cases, giving rise to no symptoms during life, fibrous adhesions and a firm, thickened, and fatty cap-

sule will be found surrounding the abscess at the autopsy. This capsule may be so tough and adherent that some force is required to separate it from the proper capsule of the kidney.

Where the clinical signs are inconclusive, unilateral disturbance of the renal function (indigocarmine test), the unilateral presence of bacteria (especially staphylococci), and a relative increase in the urinary leucocytes on the one side, permit a direct diagnosis of perinephric abscess. All 3 of these tests must be made, single examinations not being conclusive. Presence of *B. coli* in the renal urine almost certainly excludes a primary perinephric abscess. K. Scheele (Zeit. f. Urol., xviii, 369, 1924).

PROGNOSIS.—If the abscess points externally in the lumbar region the prognosis, though favorable, should be a guarded one. It is always unfavorable if it ruptures into the peritoneal cavity, groin, bowel, or bladder.

TREATMENT.—The treatment is in all cases surgical and calls for **free incision and drainage**.

Of 36 cases collected, 25 were in males. The age of the oldest patient was 60 and of the youngest, 10. Thirty-five abscesses were **evacuated**; 1 patient declined operation; 30 patients recovered and 5 died—a mortality of 14.3 per cent. M. B. Miller (Annals of Surg., Mar., 1910).

Of 11 cases of perinephric abscess, 8 were right-sided. Six were metastatic, 4 of renal origin, and 1, an extension from inflamed retrocecal appendix. Two patients had recently sustained an injury. **Needling** was performed in 6 cases. In 2 the pus was not located; in 1 of these it was later found anterior to the lower pole, and in the other at the upper pole. **Incision and drainage** were carried out in each case, without mortality. J. Z. Mraz (Okla. State Med. Assoc. Jour., Nov., 1925).

AMYLOID, LARDACEOUS, OR WAXY KIDNEY.

It is an open question whether this condition should be considered separately, since it is but a local manifestation of a widespread process due to various causes: syphilis, tuberculosis, etc. It also appears as the manifestation of the degenerative process of advanced Bright's disease, especially in the form following low fevers. It has already been alluded to in the article on BRIGHT'S DISEASE, Vol. I.

SYMPTOMS.—The condition itself may not present distinct clinical features. There is usually found a history of long-continued suppuration, or of syphilis; perhaps of alcohol. The urine generally gives very fairly characteristic indications. Its quantity is increased, its specific gravity is somewhat, but not greatly, diminished, varying from 1015 down to 1005. It is usually singularly clear and translucent, and on standing yields very little sediment. Under the microscope may be found a few casts, which are generally broad, hyaline, fatty, and granular. The amyloid reaction may be obtained with the hyaline casts. Serum-albumin and globulin may both be present in the urine, but a seemingly diagnostic condition, according to Salkowski and Senator, is the high proportion of globulin as compared with the serum-albumin. In later stages, when degeneration has set in, the urine becomes reduced in quantity, is mostly turbid, and then presents under the microscope the morphological signs belonging to the degenerative process. There are associated with this condition of urine anemia, debility, but not often much dropsy, with the characteristic transparent and deli-

cate complexion. There is usually degeneration of blood; often diarrhea and vomiting. Cerebral symptoms are not at all common. The arteries are usually soft, and the heart generally shows very little change. Death comes by wasting, diarrhea, inflammation, and the kindred affections of the liver and other organs (W. M. Ord).

DIAGNOSIS.—The diagnosis cannot usually be made from the urinary examinations alone. But if following syphilis, tuberculosis, or chronic bone suppuration, the urine is found to be albuminous, of low specific gravity, and increased in quantity, and the liver and spleen are enlarged, the diagnosis of amyloid disease may be made with comparative certainty.

ETIOLOGY.—Amyloid kidney is usually associated with amyloid degeneration in other organs, as the liver and spleen, as is the result of wasting diseases, tuberculosis of the lungs or intestines; syphilis, especially tertiary; chronic bone suppuration, or other chronic suppurative processes, as chronic empyema, intestinal ulcers, or vesicovaginal fistulae. It may sometimes be a sequel of gout, malaria, leukemia, cancer, or chronic valvular insufficiency.

PATHOLOGY.—Macroscopic examination shows the kidney to be firm, large, smooth, and pale, greenish or yellowish white, and the surface smooth, shiny, and often mottled when the stellate veins are prominent. The capsule is thickened, but is easily detached. Upon section the surface appears homogeneous, anemic, or "bacon-like," particularly in the cortical region, which is wider than normal; the pyramids are deep red in color and slightly infiltrated.

The Malpighian tufts, which are the parts most affected by the waxy change, are translucent. An application of Lugol's iodine solution to the amyloid areas will produce a mahogany-red color. If then a weak dilution of sulphuric acid is applied, a blue or violet tint is produced; if a 1 per cent. solution of methyl violet is used instead, a red color appears.

Accompanying this degeneration is a diffuse nephritis,—with fatty degeneration affecting the epithelium of the tubes especially,—glomerulitis, and thickening of Bowman's capsules. The advanced cases show marked atrophy of the secretory structures. The small, granular kidney is less subject to amyloid infiltration than the large, white kidney.

Cardiac hypertrophy does not always coexist with amyloid renal disease.

PROGNOSIS.—This depends to a great extent upon the disease which is the cause of the amyloid condition, but is usually very grave. In marked cases death occurs after a period varying from several weeks to several months.

TREATMENT.—The original disease is to be treated according to indications, while the kidney trouble will be best met by the remedies and general **dietetic** and **hygienic measures** used in chronic Bright's disease (*q.v.*, Volume II). **Iodide of iron** may be used for its alterative effects, and palatable and easily assimilable **fats** (cream, butter, olive oil) and **tonics** deserve trial. **Creosote** and its preparations are indicated in tuberculous cases; **mercurials** and the **iodides** in syphilitics; malarial cases improve under the use of **iron**, **arsenic**, and **quinine**.

SYPHILIS.

Syphilis of the kidney is usually a tertiary manifestation of lues, although it may appear in the secondary stage.

SYMPTOMS.—Except in amyloid degeneration of the kidney there are no proper symptoms that are pathognomonic of this condition.

A special form of renal syphilis has been described by Wagner, who calls it acute syphilitic glomerulonephritis, having hematuria as a distinctive feature, and a rapid end with uremic symptoms.

It is still uncertain whether the disease is the result of the action of toxins, or of a settlement of spirochetæ in the kidney. The serum reaction is always well marked. R. Bauer and P. Habetin (*Wiener klin. Woch.*, July 3, 1913).

The writer has found congenital syphilis of the kidneys relatively frequent at necropsies. The manifestations are sclerotic atrophy, gummas, and retention cysts. The condition is not characteristic of congenital syphilis, but in some instances occurs in an acute interstitial and parenchymatous form or as a condition of chronic sclerous atrophy. Canelli (*Pediatrics*, May, 1918).

PATHOLOGY.—Three forms of syphilitic infection of the kidney are observed: amyloid degeneration, which is the commonest form; chronic interstitial nephritis, and gumma.

TREATMENT.—The treatment is that of the primary disease (syphilis).

Cure of the syphilitic nephritis which may be superimposed upon an already impaired kidney, and is characterized by a specific alteration of the glomeruli, is best accomplished by a carefully combined **mercury** and **salvarsan** treatment. E. Hoffmann (*Deut. med. Woch.*, Feb. 20, 1913).

The importance of this subject has been often overlooked. There are 2 types: (1) Early involvement, which may consist in a transient albuminuria, or acute or subacute nephritis. (2) Later involvement, which may be (a) chronic interstitial and parenchymatous nephritis; (b) amyloid kidney, or (c) gumma. Acute nephritis may occur even before the skin eruption of syphilis appears, or may occur 3 years after; the average time, however, is 5 months after the infection, and it rarely occurred after the first year. The first symptom is usually edema, which may go on to general anasarca, ascites, and hydrothorax. In some instances there is pain in the lumbar region, fever, and vomiting. The most striking feature is an enormous quantity of albumin in the urine. Casts of all kinds may be present. Examined with the polariscope, double refractile lipoids are more abundant in the urine in syphilis of the kidneys than in other renal conditions. Yet renal function is less impaired. The prognosis of the early transient form is good, fairly favorable in the acute and chronic forms; unfavorable in amyloid kidney, and favorable if recognized clinically in gumma. The treatment is both specific and general. Lloyd Thompson (*Med. Rec.*, May 8, 1920).

TUBERCULOSIS.

DEFINITION.—This may be primary or secondary, the latter being the more frequent form. It may affect one or both kidneys, but generally remains unilateral for some years before the other kidney is involved.

SYMPTOMS.—There may be either no renal symptoms or none until late in the disease, but the symptoms of pyelitis are usually present. For a considerable time pyuria may be the only symptom; this usually indicates cystitis, but with that condition vesical tenesmus and frequent

micturition are associated. There is usually pain referred to the affected side, often like that of renal colic. Hematuria is not infrequently met with; indeed, it may be the initial symptom. In 203 cases Braasch found bladder irritability in 86 per cent., and hematuria in 60 per cent. Tuffier suggests the use of the cystoscope in order to trace the origin of the hematuria. Tubercle bacilli are often found in the urine, but not in the miliary form. Polyuria and albuminuria are sometimes present. The urine may also contain tube-casts, but more often pus-cells. Cheesy masses of appreciable size are occasionally seen in the urine.

When the affection becomes advanced, chills, fever of a suppurative type, emaciation, and progressive asthenia appear. An extensive lesion may exist, however, without giving rise to marked general symptoms. Tuberculous lesions, especially of the lung, are often coexistent.

DIAGNOSIS.—This is easily made if tubercle bacilli can be found, or if tuberculosis of the lungs or other organs are associated with the renal trouble. The tuberculin test will aid diagnosis. Chevassu recommends the antigen reaction of Debré and Paraf. Inoculation experiments with the urine may be made on animals, but the bacilli may reach the urine from more distant parts than the kidney. Ureteral catheterization may decide which kidney is involved when hematuria is a prominent symptom. The use of the X-ray after injections of 20 c.c. of a 10 per cent. solution of collargol into the ureters is of diagnostic aid. The phthalein test has shown greater reduction of output in unilateral tuberculosis than

in nephrolithiasis. Injection of indigocarmine will generally show which side is affected. From calculous pyelitis tuberculous nephritis may be differentiated by the facts that in the latter the pain is less severe, the tumor-mass smaller, and the hemorrhage less frequent.

The Bloch method of inoculation of guinea-pigs (injection in the inguinal region, after slight injury to the inguinal glands by compression) is advised by Keene and Laird. The diagnosis may thus be made in at least 77.3 per cent. of the cases in 10 days, as compared to 6 weeks by the subcutaneous or intraperitoneal methods.

A patient with occasional attacks of unexplainable acute pain or fairly constant dull pain in 1 loin and whose urine shows a little blood and a few leucocytes should be advised of the importance of rest and of building up his resistance, as the condition may be incipient renal tuberculosis, curable with proper care. A. L. Chute (*Jour. of Urol.*, May, 1921).

Cystoscopy shows peri-ureteral edema, soon followed by tubercles which pass into superficial ulcers. Either of these findings, in a case with acid pyuria negative to culture and containing red cells, justifies a diagnosis of renal tuberculosis. Mraz (*Jour. Okla. State Med. Assoc.*, Dec., 1922).

The value of demonstrating bacilli in the urine has been overestimated. Tubercle bacilli readily penetrate an inflamed kidney even though it be the seat of no infection. Of diagnostic value, however, are: A progressive tendency of the morbid process and infection of the bladder, to be established cystoscopically. The points of predilection are the ostium, vertex and the mobile parts of the bladder, all affected early. A. Hübner (*Deut. med. Woch.*, May 4, 1923).

In children polyuria with a light-colored and cloudy urine, lumbar pain, pollakiuria and cystalgia call for immediate examination of the urine for tubercle bacilli. P. Mathieu (*Paris méd.*, July 19, 1924).

In 100 cases discussed, the diagnosis was based on the finding of tuberculosis elsewhere in the body, the presence of tubercle bacilli in urine of low specific gravity containing varying amounts of pus and blood, and the routine urologic study. G. J. Thomas (*Minn. Med.*, Jan., 1926).

ETIOLOGY.—Age and sex are prominent factors. Most cases occur in middle life, though they may occur earlier or later. Males are more frequently affected than females.

The causative agent is the tubercle bacillus, which reaches the kidneys in the blood-stream, producing primary tuberculous nephritis, through the lymphatics and by direct extension from adjacent structures.

PATHOLOGY.—The calyces and apices of the pyramids (papillæ) are the initial location of the tubercles, from whence they extend to the pelvis of the kidney, so that early the condition may be pyonephrosis. The process then affects in turn the ureters, bladder, and prostate. In rare cases the process apparently originates in the bladder or prostate and extends upward. The tubercles, after becoming deposited in the various locations, pass through the same changes as elsewhere—caseation, necrosis, and suppuration—and in the course of these changes the renal tissue is destroyed to a greater or less extent, entailing the formation of cheesy cysts, often impregnated with lime-salts. When the bacilli reach the kidney through the blood-stream (hemogenic infection) the process may be limited to the cortex, and produce nodular tuberculosis with cheesy masses with but slight loss of the kidney tissue. It is generally conceded that the infection of the kidney is almost always hematogenous;

nevertheless, in a small number of cases renal tuberculosis is undoubtedly an ascending process. For a considerable period the disease is unilateral, though in most instances both kidneys become involved. Hallé and Motz in 132 cases found a single kidney involved in 89 cases. Disseminated tubercles in both kidneys are found in acute miliary tuberculosis, but here caseation and necrosis seldom occur.

PROGNOSIS.—Most cases of unilateral renal tuberculosis become bilateral if not suitably treated. The prognosis thus depends upon the promptness with which the condition is recognized and surgical treatment applied.

Wildbolz found that without intervention most patients with tuberculosis of the kidneys die in the course of five years. About 20 per cent. live from five to ten years, and those who live beyond ten years are very few. In a series of 168 non-operated patients the writer found that 53 per cent. had died, and 47 per cent. were living; 11.3 per cent. died the first year; 23 per cent., between the first and fifth year; 15.9 per cent., before the end of the tenth year, and but 3 per cent. lived beyond the tenth year. The average age which men live is four years and ten months, while the average that women live is five years and five months. Raffin (Jour. d'Urol., Oct., 1912).

An unusual complication of renal tuberculosis is *closed pyonephrosis* (pyonephrosis tuberculosa occlusa of Zuckerkandl), which develops after an obliteration of the renal pelvis or ureter.

The perirenal and periurethral interstitial tissue can also be affected, and at times a cold abscess is formed along the psoas, suggesting an affection of the spine (Smirnow).

Closed pyonephrosis presents greater difficulties in certain cases for diagnosis than any other condition of the kidney. In the majority of cases there is a renal distention showing itself by a lumbar or abdominal swelling. In a smaller number there is no swelling, and the affected organ is atrophic. The cases can be divided into the following groups: 1. The bladder is tuberculous. In the region of the supposedly diseased kidney a large tumor, the pyonephrotic sac, is found. The ureter on this side is impermeable. Diagnosis is easy. 2. The bladder is normal. One ureter is impermeable and on this side there is a tumor in the kidney region. Diagnosis is possible from the history of the case, and the symptoms referable to other organs. 3. The tuberculous involvement of the bladder is far advanced and cystoscopy is impossible. An enlarged kidney can be palpated. Diagnosis is possible only by exploratory incision. The enlarged kidney may be healthy and only hypertrophied, while the other kidney is atrophic and tuberculous. H. A. Fowler. (Jour. Amer. Med. Assoc., Jan. 3, 1914).

TREATMENT.—Where but one kidney is diseased, its **surgical removal** at the earliest practicable time is definitely indicated, as there is at present no evidence of a curative result from medical treatment, and the more time is lost the greater the chance that the infection will have passed to the opposite kidney or the ureter and bladder. If pus and bacteria have already been found, however, in the urine from both ureters, or where the patient with unilateral involvement refuses operation, nephrectomy is contraindicated, and medical measures will have to be depended on. (According to Hunner, where one kidney is so diseased as to be largely devoid of function while

the activity of the other is only slightly curtailed, removal of the former usually results in increased function of the latter.) The general treatment should be that appropriate for tuberculosis of the lungs, including a **generous diet** of nourishing food, **fresh air, rest, and proper hygiene**. In patients who react well **cold baths** in the form of a sponge, shower, or plunge are beneficial. **Woolen underclothing** should be worn by preference.

Results of surgical treatment in 611 cases. As a rule, **complete lumbar nephrectomy** was performed. In a few, however, **transperitoneal nephrectomy** was resorted to. Peritoneal contamination markedly increases the operative risk, as does also simultaneous nephrectomy and drainage of a perinephric abscess. Two of 8 patients died following such procedures. None of 8 patients died from a 2-stage operation. In 18 cases of bilateral infection one kidney was removed. Four died from anuria immediately after the operation, and 10 during the next 18 months. Altogether, 31.2 per cent. of the 611 are dead; 58.6 per cent. are completely cured on an average of 4 years after operation, and 10.1 per cent., still having urinary trouble. Judd and Scholl (*Ann. of Surg.*, May, 1924).

As regards medication, **tuberculin** has been used by many in an attempt to cure the disease in its early stages. At best the results obtained hardly seem to justify any delay on this account in operable cases. Symptomatic treatment in the unoperated cases consists in controlling fever with **cold sponging**, correcting constipation or diarrhea by changing the **diet** and giving **laxatives** or **bismuth**, and preventing night-sweats by **sponging with 25 per cent. alcohol or diluted vinegar** and the administration of drugs such as **agaricin, camphoric**

acid, and atropine. Hematuria, when observed, indicates the use of **morphine, calcium chloride or lactate, gelatin**, and the repeated injection of **horse serum**, 150 minims (10 c.c.) at a dose. In complications such as cystitis, pyelitis, paranephritic abscess, and uremia, the measures described elsewhere as appropriate for these conditions should be availed of.

Small doses of **tuberculin**, $\frac{1}{75,000}$ mg. twice weekly, advised. At times he gives but $\frac{1}{750,000}$ mg. The patient should feel better immediately after the first dose and for from 2 to 4 days; another dose should then be given. This treatment was used in conjunction with hygienic and symptomatic treatment, the duration of treatment averaging $3\frac{1}{2}$ years. Dillingham (*Calif. State Jour. Med.*, xv, 70, 1917).

Two advanced cases with tuberculosis of the right kidney and bladder following removal of the left kidney were much benefited by **chaulmoogra oil** or its derivatives. In 1 the treatment consisted at first of daily bladder instillations of 10 c.c. of the oil together with 15 c.c. by mouth 3 times daily. Later, intramuscular injections twice weekly of the **ethyl ester extracts of the fatty acids** of chaulmoogra oil were given in doses of 1 c.c., gradually increased to 6 c.c. The second patient received tri-weekly injections of 5 c.c. of the extracts. Cowen (*Urol. and Cut. Rev.*, Dec., 1922).

NEPHROLITHIASIS.

SYNONYMS.—Renal calculus; renal colic; gravel; pyelitis calculosa.

DEFINITION.—A condition in which fine or coarse concretions are formed in the kidney-substance or in the pelvis of the kidney by the precipitation of solid substances from the urine.

SYMPTOMS.—Pain and hemorrhage are the most important symptoms, in case the stone is small and

the kidney healthy; indeed, these may be the only symptoms present. The pain is usually felt in the loin over the affected organ; it is of a dull, heavy, dragging character. Hematuria is generally remittent; the amount of blood passed is not great; it is thoroughly mixed with the urine, and the blood-cells are altered. A larger calculus, producing suppuration, is suggested by pus in the urine with pain on pressure and perhaps increased resistance in the loin. A calculus blocking the ureter and producing hydronephrosis is suggested by feeling a soft, elastic tumor of variable size through the abdominal walls or in the lumbar region; but this is apt to disappear simultaneously with the passage of a large amount of urine. The attacks usually recur and the urine becomes alkaline or putrid. Vesical irritation, pain, retraction of the testes, and gastric disturbances are other symptoms frequently met with in all forms of renal calculus. In case of renal colic there is acute suffering, the pain shooting down the ureter to the testicle or labium majus and often radiating to the thigh. There may be nausea and ineffectual vomiting, vesical tenesmus, faintness, cold sweating, and even collapse. Oftentimes the pain ceases as suddenly as it began; but relief is not permanent unless the stone has receded into the pelvis of the kidney or has passed into the bladder. The paroxysms of pain recur at intervals of from a few minutes to several hours or days.

In a personal case there were calculi in both kidneys; the size of the calculus was $3\frac{1}{4}$ inches by 2 inches by 2 inches. There was comparatively little discomfort and pain, considering the size and irregularity of

the stone; both kidneys were found healthy at the operations. The calculus was broken into two large fragments and one small one, articulating by facets, and in a way resembling a knee-joint with patella. The joint was movable in a front to back direction, and was flexed whenever the patient bent her back. Ord (Brit. Med. Jour., Aug. 20, 1910).

The stone may remain in the kidney and prostate many years without producing any pain. In 10 per cent. of the writer's cases pain had been entirely absent at all times. Renal colic was present in only half the cases. Pain, when present, had been attributed to the urethra and its appendages, movable kidney, sacroiliac disease, appendicitis, and biliary colic. Abnormal urine is a most constant sign of renal and ureteral calculi. Albumin was present in 82 per cent.; pus in 42 per cent.; blood in 80 per cent. H. Cabot (Amer. Jour. of Urol., Jan., 1912).

The following points are emphasized by the writer: Early and careful urological examination of all patients suffering with pain in the back, in order that the diagnosis may be made early. In some cases there were no symptoms, and in many the only symptom was a dull ache in the loin, relieved by rest. The urine may show a few pus and blood cells, or be negative or full of pus. The X-ray is almost infallible in the diagnosis. Hutchinson (Can. Med. Assoc. Jour., x, 250, 1920).

DIAGNOSIS.—In the differential diagnosis from stone and malignant or villous growths of the bladder the imperfect mixing of the blood with urine, the larger amount of blood, less altered blood-cells, the presence of clots, and more severe pain would be of aid. In the case of malignant growths of the kidney the cachexia and the palpation of a tumor, possibly irregular in outline, are of use in establishing a diagnosis.

New sign for the diagnosis of latent nephrolithiasis, *viz.*, a severe pain produced by deep percussion in the lumbar region while the patient is standing, sitting, or slightly bent forward. The author strikes with the external or ulnar margin of the hand along the dorsolumbar region from the 8th vertebra downward. The blows cause a stab-like pain when the affected organ is reached. This sign proved useful in numerous cases. Goyena (*Presse méd.*, Jan. 7, 1925).

The Röntgen rays enable us to detect renal calculi with accuracy as to their number, size, and relative position. Calculi of calcium oxalate give the most distinct pictures, those formed of urates are less easily recognized, and phosphatic calculi are most difficult to photograph. Injection of collargol through an opaque sound previously introduced into the renal pelvis permits of outlining by X-ray the pelvis and calyces.

In 42 cases, including 10 bilateral, the stones were revealed by the X-rays in 29; in 4, not shown by X-ray, stones were later passed, and in 2 they were found at operation. *Physical examination* is of value mainly in excluding other conditions. *Cystoscopy* was negative in the majority of cases. A *carefully taken history* is the first essential, giving clues to the existing condition. Previous to X-ray examination $\frac{1}{2}$ ounce of castor oil should be given on the morning and evening of the preceding day, with fluids but no milk that day and no breakfast on the day the plate is made. Frequent urination is the commonest symptom; pain varies from a dull ache to colic. Function is usually depressed on the affected side. There is no objection to a *pyelogram* if the shadow-casting fluid can be drained off. G. W. Hartman and S. A. Goldman (*Calif. State Jour. of Med.*, Feb., 1921).

Not every shadow in the kidney indicates a stone. Differentiation is made by the appearance of the shadow,

the use of *X-ray catheters*, and *pyelography*, between kidney stones and calcified lymph-nodes, gall-stones, pancreatic calculi, or calcified areas in a tuberculous kidney. Pyelography is valuable in showing that the shadow is that of a renal calculus, completely covered by the pyelogram, and in revealing the degree of dilatation of the kidney pelvis and consequent destruction of parenchyma. Uric acid or cystin calculi give very faint shadows; various *silver salt solutions* will intensify such weak shadows. Eisendrath (*Internat. Clin.*, iv, 246, 1922).

Uric acid stones may be demonstrated by Kummel's method of *impregnation with collargol*, by *air inflation* of the renal pelvis, and by *pneumoradiography* of the kidney bed. As stones immersed in fluid may be invisible, a second examination should be made after the residual urine has been emptied from the renal pelvis and bladder. Concretions smaller than a caraway seed may cause typical colic and hematuria. V. Blum (*Zeit. f. klin. Chir.*, July, 1922).

The X-ray is at times the only diagnostic resource. The author noted concretions in the kidneys of 9 patients, out of 46 operative cases, in whom pain was absolutely absent. In cases with an old history suggesting the possibility of renal calculus, or in hematuria with an uncertain diagnosis, and in pyuria, only the X-ray may reveal the renal cause of these phenomena. R. Lanzillotta (*Jour. d'urol.*, June, 1924).

Calcium oxalate and calcium phosphate give very good shadows, and are very common constituents of urinary calculi. The high relative opacity is due to the high atomic weight of the calcium present in these salts. All the other common urinary salts give relatively poor shadows. They include the urates, uric acid and triple phosphate. Cystin and xanthin also give poor shadows in the pure state, but of slightly more opacity than the foregoing, owing to the sulphur they contain. H. P. W. White (*Brit. Jour. of Surg.*, July, 1924).

ETIOLOGY AND PATHOLOGY.

—Renal calculus occurs most frequently in males, before the age of 15 and in the later years of life. The uric or lithic acid diathesis (lithemia), gout, an excessive meat (protein) diet, and a sedentary life apparently predispose to nephrolithiasis. Its formation depends upon the gluing together of crystalline particles or amorphous salts in the urine by colloid material from blood-clot or mucus. The masses thus formed vary in size from sand to that of a hen's egg; some of them assume the shape of branches of coral. The nuclei of calculi are said to consist most commonly of ammonium urate in children, uric acid in adult life, and calcium oxalate after the fortieth year. The phosphates, cystin, and xanthin less frequently give rise to renal calculi.

A small stone may be lodged in healthy renal tissue, giving rise, perhaps, to bleeding, congestion, and inflammation and various nervous symptoms; or, it may cause the formation of an abscess in the substance of the kidney. Gravel may pass from the uriniferous tubules and be carried away by the current of urine without causing symptoms. A small stone may pass along the ureter with difficulty, causing renal colic; it may remain a movable body in the pelvis, by its irritation producing pyelitis, or by stopping the ureteral orifice produce hydronephrosis; or, it may be lodged in the pelvis or calices, forming a large, sometimes branched calculus, and give rise to inflammation, suppuration, and thickening of the tissues about it.

In some parts of the world infantile lithiasis is practically unknown. In Hungary and in the central part

of Russia along the Volga it is quite common. Von Bókay (*Zeit. für Kinderheilk.*; *Med. Record*, Aug. 2, 1913).

Kidney pain may occur in cases of stricture or obstruction of the ureter at the ureteropelvic junction by aberrant vessels, renal tumor, fascial bands, etc., ureteral obstructions from tumors in the abdomen and pelvis (*e.g.*, uterine fibroids, cancer of the cervix uteri, etc.); certain bladder lesions, *e.g.*, benign and malignant growths, diverticula, etc.; seminal vesiculitis; inflammatory conditions of the broad ligaments and of the appendix; obstruction of the urethra by stricture and prostatic hypertrophy. S. H. Harris (*Med. Jour. of Australia*, Jan. 18, 1919).

PROGNOSIS.—The passage of gravel without marked symptoms tends to recur or persist, and subsequent formations are apt to be larger and cause alarming symptoms. A fatal issue may follow an attack of renal colic. Large latent calculi of long standing generally lead to such conditions as pyelonephritis, pyo- and hydro- nephrosis, perinephritic abscess, and uremia. The prognosis should always be a guarded one.

TREATMENT, MEDICAL.—During the attack of colic the patient is to be given the **hot bath** and **hot drinks of lemonade or soda-water**, while **hot fomentations** are to be applied to the **loins**. If these measures are insufficient to bring relief, **morphine** and **atropine** or even **chloroform** may be used.

Lying in bed usually prevents recurrence of hemorrhage. If the bleeding is excessive, operative measures are the only resource. A constant dull pain may get transient relief from mild narcotics, but **glycerin** is more effective, a tablespoonful every three hours up to 150 c.c. (5 ounces), with a little tincture of bitter orange peel and tincture of gen-

tian to prevent nausea. L. Casper (Med. Klinik, Oct. 6, 1912).

To aid in expulsion of calculus from the kidney by far the best treatment is: **Spirit of turpentine** in 10-minim (0.6 c.c.) doses in gelatin capsule *t. i. d.* **Diet** of milk, each tumbler diluted $\frac{1}{4}$ part with water, milk to be slightly warmed and drunk slowly. Fish and dry toast may be taken once daily. The patient is to **rest recumbent** during the regimen and to take occasional **hot sitz baths**. The treatment to last six days consecutively, then after a two-day interval it is repeated once or twice, if necessary. F. S. Watson (Boston Med. and Surg. Jour., Jan. 9, 1913).

The writers employed their method of **non-operative removal** of ureteral calculi in 31 cases during the past 3 years and have been compelled to operate upon only 2 of the patients. The treatment consists in first passing a No. 5 bismuth catheter into the ureter until it meets resistance. A röntgenogram then will show the location and size of the stone. Then 2 c.c. ($\frac{1}{2}$ dram) of a 2 per cent. solution of **cocaine** are injected slowly at the site of the impaction and 3 or 4 minutes later the catheter is passed beyond the stone and 10 c.c. of **sterile oil** are injected. If the catheter cannot be passed beyond the stone the oil is injected with some force to dislodge the stone. The patient is then kept well under the influence of **morphine**, drinks water to assist in expelling the stone, while **hexamethylenamine** is administered. The treatment is repeated every second or third day until the stone is expelled, a larger catheter being used each time to dilate the ureter. Crowell and Thompson (Jour. Amer. Med. Assoc., Aug. 10, 1918).

Between the attacks attention must first be directed to hygienic and dietetic measures. **Moderate exercise** is to be taken daily **in the open air** and the patient is to lead as **quiet and temperate a life** as is possible. Over-eating of **red meats** and of nu-

cleoproteins (liver, sweetbread) and indulgence in **alcohol** should be **prohibited**. Large quantities of **water**, either **mineral**—such as **lithia**, **Poland**, **Carlsbad**, and **Vichy**—or **distilled**, are to be taken daily. **Bicarbonate or citrate of potassium** given in 1-dram doses in a tumblerful of water two or three times daily, or **benzoate or carbonate of lithium** in 5-grain doses three times a day, is of value. **Piperazin** has been claimed by some to be a solvent for uric acid calculi and may be exhibited in 5-grain doses three or four times daily. Von Noorden and Strause advise the use of **calcium carbonate** in doses of from 10 to 20 grains (0.65 to 1.3 Gm.), thrice daily. They believe that the calcium combines with the acid phosphates in the intestines, and thus reduces the deuterophosphates in the urine, leaving the protophosphates to dissolve the uric acid.

The **urine** should be **kept faintly acid**, the reaction being tested at intervals for that purpose. The **alkaline** treatment must be temporarily suspended if the urine becomes **alkaline**; otherwise, a secondary deposit of phosphates around the uric acid stone is favored. Lumbar pains call for occasional doses of analgesics, such as **phenacetin**, **belladonna**, **hyoscyamus**, **codeine**, and **diuretics** (**spirit of nitrous ether**, **buchu**, and **uva ursi**). Renal hemorrhage demands the use of **ergot** or the astringents, **alum** and **gallic acid**. When the calculus is composed of phosphates or of calcium carbonate the urine should be made **acid** through the use of **saccharin** or **benzoic or boric acid**. When the hemorrhage persists or the stone is of such dimensions or shape that it cannot be passed, etc. (see next article: KIDNEYS

AND URETERS, SURGERY OF), either **lithotomy** or **litholapaxy** may have to be resorted to.

In acute renal colic, the use of **morphine** and **atropine** hypodermically followed by 2-ounce doses of **glycerin** with large quantities of **distilled water** are of value in aiding the passage of stones spontaneously, especially if the patient is in a very **hot bath**. The diagnosis may be confirmed by careful urine examination by the X-ray, by introduction of ureteral shadow sounds, and by pyelography in doubtful cases. A. J. Ochsner (N. Y. Med. Jour., June 14, 1919).

Direct dissolution of a stone in the renal pelvis with 0.8 per cent. **hydrochloric acid** was attempted without success. Upon surgical removal, however, it could be crushed in the fingers after being placed in the patient's urine, acidulated with hydrochloric acid to 0.5 per cent., for 36 hours. Only 13 per cent. of stones would permit of dissolution *in situ*, consisting mainly of carbonate and phosphates. R. C. Bryan and R. D. Caldwell (Jour. of Urol., Apr., 1922).

Where stones cause chronic pain, the writer uses a mixture of **glycerin**, 150 Gm. (5 ounces), and **bitter tincture** and **tincture of orange**, of each 5 Gm. (1½ drams). One tablespoonful is given every 3 hours. Where infection of the renal pelvis persists, he recommends free use of **water**, including **mineral waters**, by the mouth, especially at night, and **irrigation of the renal pelvis** with 1 or 2 per cent. **silver nitrate solution**. Israel (Berl. klin. Woch., Dec. 16, 1922).

The writer advises **removal** of a single, unilateral stone lying in the renal pelvis which has caused 1 or more attacks of pain or is accompanied by signs of infection. A large branching calculus or multiple calculi should be removed if renal function tests and pyelogram indicate little parenchymatous destruction. He also operates, preferably at 2 sittings, in bilateral calculi with well preserved function but with accompanying infection. One

should not operate in bilateral cases if there is little parenchyma left and especially if there is still much infection; recurrence is apt to be rapid in such cases. A ureteral calculus completely blocking the opposite kidney should always be removed before attempting removal of a renal stone. Recurrence occurs in 15 to 20 per cent. of cases, either because of overlooking calculi or of true reformation. The operation of choice is **pyelotomy**, which succeeds in a majority of cases, especially if combined with a small **nephrotomy** incision. **Nephrectomy** should be performed only where the opposite kidney is intact and the involved organ hopelessly destroyed. Eisendrath (Internat. Clin., iv, 246, 1922).

In 2 cases, the kidney was drawn out and the X-ray plate, wrapped in black paper, placed in front of or behind it. The patient was then wheeled into the X-ray room. In 10 minutes the finished picture cleared up the diagnosis of renal calculi. Reschke (Deut. Zeit. f. Chir., May 1924).

If the stone is associated with **cystinuria**, disintegration should be attempted by internal administration of **alkalies**, **pelvic lavage with alkaline solutions**, and **limitation of protein diet**, as was done in 1 case observed. A. J. Crowell (Jour. of Urol., June, 1924).

A stone will be affected by **distilled water** only if it is a urate or oxalate stone, and of small size. Even in patients to be operated on it is advantageous, however, when there is infection. It may also keep the patient in good condition without operation for a long period. Rovsing (Acta chir. Scandin., Oct. 18, 1924).

Pituitary extract injections employed to promote the elimination of small stones. In cases with infection **methenamine** should be given beforehand. Furthermore, the presence of stones of excessive size should be excluded by X-ray examination. Colic begins in 15 to 30 minutes after the pituitary injection and is mitigated by giving morphine. Kalk and Schöndube (Deut. med. Woch., Jan. 8, 1926).

HYDRONEPHROSIS.

DEFINITION.—A collection of urine in the pelvis and calices of the kidney due to obstruction.

VARIETIES.—In addition to the usual or more or less typical form, two subvarieties are distinguishable: (a) the intermittent, and (b) hydronephrosis paraplegica. In the latter type paraplegia develops as a complication, and beyond the mention of this fact it scarcely deserves a separate clinical description.

SYMPTOMS.—The clinical symptoms are somewhat dependent upon the cause and stage of development of the hydronephrosis. When, as generally happens, the condition is unilateral, it often escapes notice, since the symptoms are slight or even wanting, until a tumor is discoverable. The ureter on the opposite side may become obstructed, followed by uremic manifestations, the latter occurrence first inviting attention to the condition. In the bilateral form the uremic symptoms are apt to supervene early.

The flow of the urinary fluid may be noticeably diminished, though subject to variations. The patient may complain of frequent and acute pains that shoot about the affected loin-space and downward toward the thigh. Abnormal sensations of weight and a dragging discomfort, at times amounting to a dull, aching pain, are quite common. The latter symptom, particularly in large hydronephrotic tumors, may be continuous and distressing; less often there is no pain.

The tumor may cause obstinate constipation from pressure on the colon, or it may, if moderate in size, provoke diarrhea, from the pressure irritation. Resulting from the same

cause are flatulency and irregular bowel action. Among gastric symptoms, anorexia is the most common, while nausea and vomiting are sometimes associated. Hematuria may be present, but is rare and usually occurs with attacks of pain.

A hydronephrosis may be an underlying cause of attacks of acute abdominal pain. In cases due to constant mechanical obstruction to the ureter, a complete uranalysis as a rule reveals no pathological findings and X-ray examination of the kidney and ureter will also generally prove negative. S. P. Martin (N. Y. Med. Jour., May 4, 1918).

Slight albuminuria may be present. The urine is of low specific gravity, the urea is diminished, and the phosphates are greatly reduced in most instances. Renal casts are absent, as a rule, unless chronic nephritis coexists as a complication.

In all except the earliest stages there is easily detectable a swelling in the region of the affected kidney. It increases in size in a slow and gradual manner, and there is great dilatation of the pelvis of the kidney. Visible bulging usually occurs in the hypochondriac and lumbar regions.

On palpation, a rounded, firm, more or less elastic and sometimes fluctuating tumor is detected. The enlargement may be slightly tender. I would advise energetically that when the tumor is of moderate size it is most readily felt when the abdominal position is employed, examining bimanually. Percussion elicits dullness over the mass, except in cases in which the colon overlies it, when the note is tympanitic: a characteristic sign of renal tumors. Moderate enlargements generally do not descend during inspiration.

Intermittent Form (Landau).—In this variety decided variations in the size of the tumors occur, *i.e.*, coincident with a more or less sudden increase in the quantity of urine passed (polyuria) the tumor quickly diminishes. On the other hand, the enlargement gradually increases from retention as the flow of urine decreases. The principal cause of hydronephrosis is a movable kidney, and hence the affection occurs mostly in women that have borne children. According to Albarran, the polyuria which commonly follows the attacks of pain in movable kidney is due to excessive urinary secretion, and not to a flow of urine which has previously been retained in the pelvis of the kidney. He reports a number of cases in which an operation for movable kidney, in patients suffering from intermittent hydronephrosis, was performed by himself, and total absence of dilatation of the pelvis of the kidney was noted.

In intermittent hydronephrosis idiopathic dilatation of the kidney pelvis is the primary disturbance. Ultimately this entails kinks and distention.

In a personal case, one of intermittent hydronephrosis on the right side, X-ray examination revealed extreme dilatation of the kidney pelvis on both sides, but no symptoms from the left kidney. Attempts to dilate the ureter and rinse out the pelvis might be useful, but the only logical treatment is to transplant the ureter to the lowest part of the sagging renal pelvis. L. Bard (*Jour. d'Urol.*, ix, No. 4, 1920).

Preceding and accompanying the polyuria in these cases are colicky pains, and hematuria is not uncommon. For obvious reasons, the tumor in intermittent hydronephrosis dis-

plays considerable mobility. The general features consist merely of a certain loss of flesh and strength incident to the associated worry and anxiety. The filling of the nephrydrotic cyst, the enlargement, and the pain of subsequent discharge, with marked diminution of the tumor, recur with variable frequency. Among the causes that are apt to produce a kinking of the ureter, and thus excite an attack, are violent physical exertion; jarring or jolting, as in riding or driving, or acute gastrointestinal derangement, and strong emotions.

The duration of the attacks varies from several hours to a day, though the cyst may continue to increase in size for several days after the pain has disappeared. During the intervals, and even while the greatly increased flow of urine is present, the patient feels tolerably comfortable.

The occurrence of chills, fevers, and sweats, rapid pulse, nausea and vomiting, and abdominal distention is indicative of suppuration, and the appearance of the common sequel—pyonephrosis. This is confirmed by the cloudy urine, revealing pus, following both discharge and aspiration. Chronic nephritis may supervene, as shown by the lower specific gravity and the presence of albumin and casts in the urine. The arterial tension will then be increased, as a rule. Among other sequelæ may be mentioned acute febrile or chronic afebrile uremia, the latter having been mentioned above.

The cystoscope and ureteral catheter are important aids in the recognition of hydronephrosis to determine the character of any obstruction, torsion, calculus, growth, etc., that may be present. The X-rays are useful partly for the detection of calculi, and

more especially in the procedure of pyelography, in which opaque salts are introduced through the ureteral catheter and the exact size, position and relations of the renal pelvis thus ascertained.

The normal kidney shows dim X-ray shadows of the 2 main calyces, and of the small, slit-shaped pelvis. Sharp beginning pelvic shadows are significant of beginning hydronephrosis. Of still greater importance is the ureteropelvic junction, which in beginning hydronephrosis becomes angular in contour, while the pelvis becomes sacculated. Dilatation of the renal pelvis and of the calyces may be found independently or simultaneously. In sacculatation of the whole kidney the shadows of the calyces exceed in size that of the pelvis. M. Krotoszyner (Calif. State Jour. of Med., xv, 58, 1917).

In a boy of 9 an operation revealed that the ureter was kinked by a supernumerary artery. C. Martin-Du Pan (*Revue méd. de la Suisse Romande*, Oct., 1917).

Stress laid on the feasibility of recognizing congenital hydronephrosis early by modern diagnostic methods, which will permit often of saving kidneys otherwise doomed to destruction before early adult life. In 1 of the author's cases, a boy of 7 years, the pelvis was widely dilated but the renal substance had not yet been seriously encroached upon. A. I. Folsom (*So. Med. Jour.*, May, 1922).

The writers found it possible experimentally to reduce urinary secretion by a properly placed, partially obstructing tube on the renal artery. If this is combined with ligation of the ureter, hydronephrosis develops to a much greater degree and more rapidly than when the ureter alone is ligated. This increased rate of hydronephrotic atrophy in the presence of a reduced secretory pressure and oliguria indicates that back pressure and pressure atrophy have not quite the importance generally ascribed to them, but that another factor, a nutritional one, is an

equally or more determining one. I. F. Hinman and A. B. Helper (*Arch. of Surg.*, Nov., 1925).

DIFFERENTIAL DIAGNOSIS.—

Pyonephrosis may be eliminated in the absence of an abundance of pus-cells in the aspirated fluid and of the general symptoms of suppuration.

Echinococcic Cyst.—In this disorder there is a history of close association with dogs; the size of the tumor is constant and slowly increasing; urea is not demonstrable in the aspirated fluid. In fluid removed by puncture the echinococcus hooklets, shreds of membrane, and sodium chloride are found. A movable kidney is not detectable. The urine is constant in amount. Recurrences do not occur.

Additionally, hydronephrosis must be distinguished by exclusion from **ovarian cyst**, **cystic kidney**, and **tumors of the spleen, liver, and gall-bladder**. Very large cysts may be mistaken for ascites. The assured presence of the colon over the tumor is diagnostic, and a chemical examination of the fluid obtained by the use of the exploring needle will clear up most cases. With reference to ovarian cyst, however, it is to be recollected that a slight amount of urea is sometimes found in it.

Case in which the kidney contained 30 quarts of fluid at necropsy. The patient was a woman of 25 and the first signs of trouble had been noted at the age of 8. For years it was ascribed to tuberculous peritonitis and the hydronephrosis assumed to be ascites until finally chemical examination of the puncture fluid excluded ascites, as there was only 2.2 Gm. of albumin; experience has shown that with ascitic fluid the proportion of albumin is never below 3 Gm. per liter. Mosny, Javal,

and Dumont (Jour. d'urolog., Jan., 1913).

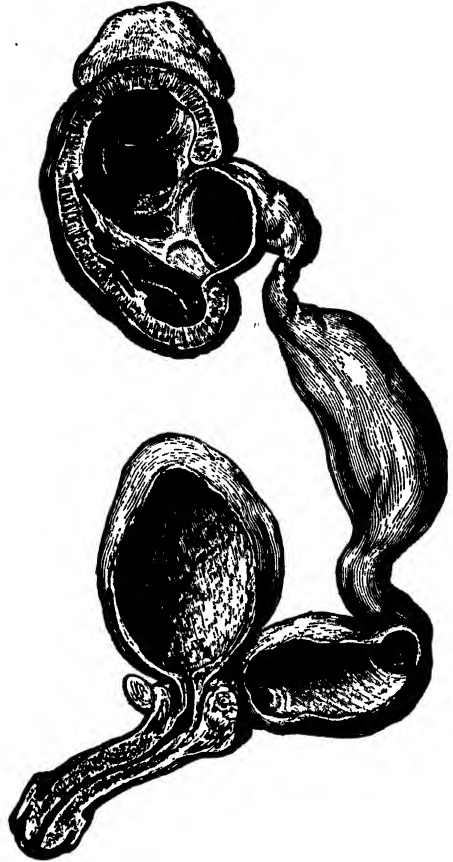
ETIOLOGY.—The principal factor in the production of dilatation of the pelvis of the kidney is chronic or prolonged obstruction, caused by occlusion of the ureter, either congenital or acquired. Probably from 20 to 35 per cent. of the cases are congenital (Roberts). The former cases are due to obstruction induced by a defective development or malformation of the ureter of one or both sides, usually the latter.

There may be atresia, a valve-like formation, or an acute (oblique) insertion of the ureter into the kidney.

Excessive dilatation has occasioned more or less mechanical difficulty during labor. The causes, both predisposing and exciting, of the acquired cases are varied, and may be conveniently grouped in tabular form as follows: 1. Sex, women being more often subject to hydronephrosis than men, especially those having borne children. 2. Age; apart from the congenital cases, hydronephrosis is most common in middle and advanced life. 3. Impacted calculi in the ureter or renal pelvis. 4. Disease of the ureteral walls, as inflammatory thickening and cicatricial stenosis from ulcers. 5. Flexion and twisting of the ureter, as from movable kidney. 6. Pressure upon the ureter from without, as by tumors and constricting bands (pelvic adhesions). The gravid and retrodisplaced uterus, uterine and ovarian neoplasms, and similar conditions causing compression or traction and obliteration of the lumen of the ureter are found in this class. 7. Diseases and tumors of the bladder that involve the ureteral orifices, particularly carcinoma, or that cause reten-

tion, as prostatic enlargement. 8. Urethral stricture.

The writer found experimentally that sudden, complete obstruction of 1 ureter produces hydronephrosis in



Urinary organs of a newborn child, showing mechanical obstruction. (Bland Sutton.)

most cases, though rarely an atrophy of the kidney develops. When hydronephrosis occurs, the venous collaterals are well developed; atrophy is due to lack of development of these. When obstruction to the ureter is partial or intermittent the hydronephrosis is of greater size than when it is complete and permanent, for in the latter case urinary secretion

ceases before the venous collateral circulation has time to develop. Barney (*Annals of Surg.*, May, 1917).

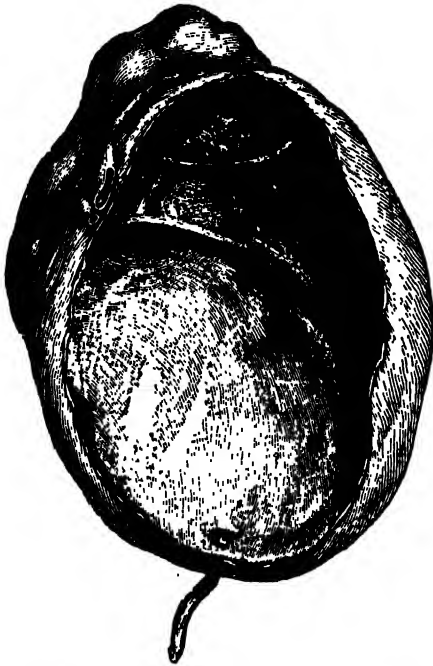
PATHOLOGY.—The cyst caused by a dilatation of the pelvis of the kidney, often assuming the shape of the latter, may become very large, containing as much as several gallons of fluid. The external appearance of the walls may be lobulated, particu-

tumor or dilatation. Accumulated liquid causes flattening and atrophy of the papillæ and gradually of the tubules and glomeruli, and in extreme cases remnants only of the renal structure remain in the walls of the hydronephrotic cyst. In the renal parenchyma (medullary and cortical) there is a growth of connective tissue, a chronic nephritis with degeneration and atrophy of the renal cells. The mucous membranes lining the pelvis and calices first become thinned, and later thickened, by the growth of connective tissue, thus forming a dense sac-wall.

The fluid contained in the sac is usually a clear, thin, yellowish, watery urine. Its composition, however, varies. The specific gravity is low, and the reaction is often slightly alkaline. Traces of albumin, urea, and uric acid are found, although in long-standing cases the latter two ingredients may be absent. Turbidity may be observed, owing to admixture with pus, blood, or epithelium, but only in instances in which previous inflammatory conditions—as a calculous pyelitis—or local complications—as hemorrhage, suppurative inflammation, and the like—have existed.

The fluid content in a closed hydronephrosis is not stagnant nor cumulative, but undergoes constant change, fresh fluid being secreted by the kidney and the excess removed through an active reabsorption, which reabsorption takes place chiefly through pyelovenous back flow. Hinman and Veckl (*Jour. of Urol.*, Mar., 1926).

PROGNOSIS.—In unilateral hydronephrosis, the more common variety, the prognosis is guardedly favorable, on account of the establishment of compensatory function on the part of the unaffected kidney, and this is



Large intermitting hydronephrosis due to an inadequate ureter. (*Bland Sutton.*)

larly in medium-sized sacs; the interior, however, shows only partial septa projecting from the walls into the cavity of the sac, as a rule. According to the site of the obstruction one or both ureters may also be dilated, and if, as is usual, one kidney is involved, its fellow is often hypertrophied. Marked enlargements cause displacement of the adjacent abdominal organs.

Atrophy of the renal tissues results and is proportionate to the size of the

particularly true if the case be one of movable kidney. The bilateral affection is always grave, having about the same outlook as chronic pyonephrosis. Among dangerous complications may be mentioned uremia and infection of the cyst by pus organisms. Recovery may ensue in rare instances in which a spontaneous discharge of the fluid occurs. Rupture of the sac is unlikely.

TREATMENT.—The congenital form, when bilateral, is not amenable to treatment. It is rarely feasible to force the fluid out by manipulation of the tumor. This method tends to remove the occlusion, when caused by a slight twist or kink in the ureter. In unilateral hydronephrosis carefully **tapping** the cyst may be practised, thus overcoming the mechanical discomfort. **Operative interference**, with a view to removing the special obstructive cause, is also to be advised in suitable cases.

In acquired hydronephrosis symptomatic treatment only is required in moderate enlargements, though sometimes gentle **massage over the sac**, properly directed and cautiously applied (to avoid rupture), may cause a reduction in the size of the cyst. In the majority of instances surgical measures only are of use. **Repeated aspiration** of the sac has, in a few reported cases, accomplished a cure. Surgical measures also embrace **nephrotomy** and **drainage**, **nephrorrhaphy** (particularly when caused by movable kidney), and **nephrectomy**.

The treatment depends on the presence or absence of another healthy kidney and the functional power in the affected organ. In 15 cases the writer performed 5 **nephrectomies**, 3 **nephropexies**, 2 **pyelotomies** for stone, 1 **pyeloplication**, and 3 **ureteropyeloplasties**.

It is necessary, after emptying the renal pelvis at operation, to keep it empty by drainage for a considerable time thereafter. Nephropexy with drainage is indicated for abnormally mobile kidneys as well as after a plastic operation. Ureteropyeloplasty is best when there is congenital stricture and the pelvic walls are not fibrosed. Pyeloplication is indicated when the ureteral orifice is of good size and situated high. Pannett (Brit. Jour. of Surg., Apr., 1922).

In no case in which the symptoms are mild, as in some instances of the intermittent variety, should surgical procedures be undertaken.

JAMES M. ANDERS,
Philadelphia.

KIDNEYS AND URETERS, SURGICAL DISEASES OF.—GENERAL DIAGNOSIS.—**Tests of Functional Activity.**—Many tests of kidney capacity have been introduced in late years. Most of these depend upon the ability of the kidney to excrete foreign substances. *Iodide of potassium*, *salicylic acid*, and other products were used at first. More lately various coloring materials, such as *methylene blue* and *indigocarmin*, have been administered. The time required for the color to appear in the urine and the total amount excreted ordinarily indicate the activity of kidney function. *Phloridzin* has been injected and gives rise to an artificial glycosuria, and the estimate of the glucose thus produced has been made.

Intravenous injection of 5 c.c. of a 0.4 per cent. solution of *indigocarmin* is advantageous as a test of renal function. With this procedure, excretion began in 3½ to 6½ minutes and the percentage output for 1 hour ranged from 34.53 to 62.97. If the dye fails to appear in 10 minutes the kidney should be regarded probably as functionally insufficient. A close parallel-

ism between the indigocarmine and blood nitrogen retention tests was shown. B. A. Thomas (Jour. Amer. Med. Assoc., Oct. 21, 1922).

The *Pregl test* is considered by the writer superior to the indigocarmine test. The specific gravity of the urine is first determined by catheterization of the ureters. The amount of solid substances excreted is estimated by using Haeser's coefficient, and compared with the weight of ash. The diseased kidney may excrete the same amount of water, but less solid material. Reduced renal function is also indicated by a predominance of the mineral substances (ash) over the organic. Even in extreme oliguria this method is serviceable. Haberer (Wien. klin. Woch., June 11, 1925).

Phenolsulphonphthalein, suggested by Rowntree and Geraghty, has the advantage of being non-irritating, non-toxic, and easily used, and it determines the activity of elimination with mathematical accuracy. From 60 to 85 per cent. of the amount used is excreted by the normal kidney in two hours, and the percentage is very simply determined by the use of the Du Boscq or other colorimeter.

In the *phenolsulphonphthalein test*, the patient is given 200 to 400 c.c. of water 20 or 30 minutes before the test. The bladder is emptied aseptically with the catheter, the time noted, and 0.006 Gm. of the chemical, in 1 c.c. of water, injected intramuscularly in the lumbar region. The catheter is allowed to remain and the urine collected from it in a test-tube containing a drop of 25 per cent. NaOH solution, until a faint pinkish tinge appears; the time is noted, and the catheter withdrawn. The patient voids at the end of 1 and 2 hours in separate receptacles, and the amount of the chemical in each is determined by means of a colorimeter, after taking the specific gravity, making the specimen strongly alkaline with NaOH, and diluting it to 1 liter with distilled water. With Rowntree and Geraghty's modification of the Autenrieth-Königsberger colorimeter

the percentage can be read off at once. Normal subjects excrete 50 to 65 per cent. of the chemical in the first hour, and by the end of the second, 70 to 90 per cent. of it should be eliminated. When renal efficiency is impaired, the output may be much smaller and the excretion delayed. A normal output does not, however, entirely exclude anatomical renal change. In impending uremia the output is usually very low. In stasis-kidney, it is somewhat reduced. By the added use of ureteral catheterization, the functional value of the separate kidneys can be ascertained.

Cryoscopy (see Vol. III) is used for determining the freezing point of a solution, and gives an absolute method of determining the total dialyzable molecules in any solution. It has the advantage of giving the capacity of the kidney to excrete all substances which should pass through them; most other methods determine only one particular substance, such as urea, the chlorides, or nitrogen, and total solid determinations are likely to be inaccurate and include albumin, if present, while cryoscopy does not. The most satisfactory method is to test the freezing point of the urines obtained by ureteral catheterization; the freezing point of the blood may also be tested.

Blood Tests.—The consensus of opinion is that these should be availed of in addition to the color tests. The phenolsulphonphthalein test will reveal changes in the kidney which have been going on but a short time, before changes in the blood occur, but it is also more apt to indicate temporary, unessential variations in excretory power (as in the marked reduction of phthalein output that may occur in bilateral calculous disease, in spite of normal blood urea), while the blood tests show more clearly the actual degree to which the system as a whole is threatened by the condition

of the kidneys, demonstrating whether the existing excretory capacity is or is not sufficient to take care of the elimination in the individual patient.

Frontz and Geraghty believe, in common with many others, that practically all the information of clinical value gained by estimations of *total nitrogen, non-protein nitrogen, uric acid* and *creatinin* is furnished by estimation of the *blood urea content*. For this purpose they use the urease method of Marshall [see HEMATOLOGY: BLOOD UREA DETERMINATION, Vol. II], which is a simpler procedure than the approved methods for total nitrogen, non-protein nitrogen, etc. Where phthalein excretion is much reduced, they add to it the blood urea estimation in order to determine the existing degree of retention, if any. Patients with increase of blood urea are far worse surgical risks than others with the same degree of phthalein excretion impairment but no excess of blood urea. According to MacLean, the normal range of blood urea is 15 to 40 mgm. per 100 c.c. of blood. Any value over 45 mgm. is suspicious and over 50 mgm. points to renal insufficiency.

The fact was pointed out by Rowntree that the saliva shows the same urea concentration as the blood. H. M. Schmitz (Jour. of Lab. and Clin. Med., Nov., 1922) investigated the possibility of instituting a clinical test in this connection. The teeth were brushed, mouth well rinsed, paraffin given to the patient to chew, and the saliva collected in a small cup containing a few drops of molecular phosphate solution. Simultaneous determinations of the blood urea and *saliva urea* in 45 miscellaneous cases showed the saliva urea averaged 89.4 per cent. that of the blood. He concluded that the saliva method may be employed when for any reason it is impracticable to obtain blood specimens. Others have confirmed the utility of this procedure.

Radioscopy (fluoroscopy) of the kidneys is a simple and rapid method of examination which is well suited for some clinical purposes. The patient should preferably be examined in the standing position, a cylindrical diaphragm used to render the picture as sharp as possible, and the soft tis-

sues compressed by means of a suitable apparatus. As stated by Braasch and Foulds, fluoroscopy has proved to be of great practical value, and no conservative operation for renal lithiasis is complete without it.

Pyelography.—It is impossible by symptoms alone to make a diagnosis of early dilatation of the kidney. Ureteral catheterization is not very accurate. Simple radiography is more definite, but kidneys vary in size and it is not possible to aver that a given kidney is enlarged. Proportional renal measurements of a series of plates carefully taken by radiography give fairly good results. The best of all methods and that which gives the most striking and accurate information is pyelography. Injection into the renal pelvis of an opaque solution yields a shadow showing the contour of this cavity.

Pyelography affords diagnostic information in a variety of renal disorders. In *pyelitis*, the renal pelvis appears dilated, with the calices smoothed off. In *pyonephrosis*, a more extensive process is shown. Otherwise unrevealed *stones* show a local thinning of the shadow of the pyelogram. In *hydronephrosis*, the size, position, extent of destruction, and usually, the etiologic lesion are shown. In *malignant disease*, the procedure reveals early a distortion and filling defect, and may thus be a life-saving measure. *Horseshoe, unilateral, infantile, and double kidney*, as well as *ureteral stricture*, are positively diagnosed by it. The main *contraindications* to it are fever, a known subacute infection, marked functional impairment of both kidneys, senility, emaciation and temporary weakness.

Graves and Davidoff disapprove of pyelography in ambulant cases. Brief drainage of the renal pelvis before the slow injection of the pyelographic medium is advised. Either gravity or the syringe may be used to introduce the latter; the main point is to avoid high pressure and overdistention. Forced fluids, rest and urinary antiseptics

should follow the procedure. Osborne, Sutherland, Scholl and Rowntree (Jour. Amer. Med. Assoc., Feb. 10, 1923) found that good roentgenograms of the kidneys and ureters could be obtained in about 50 per cent. of cases 1 hour after *intravenous injection* of 10 Gm. (150 grains) of sodium iodide. Occasionally the *liver* and *spleen* were also shown. For examination of the *bladder* (cystography) good results were obtained 1 to 2 hours after *oral administration* of 3 Gm. (45 grains) of sodium iodide hourly for 3 hours.

Twelve per cent. *sodium iodide* is the pyelographic medium of choice, but lacks the important quality of germicidal activity. For this reason the writer advocates introduction in it of 1:3000 of *mercuric iodide*, which is the equivalent of 3 to 4 per cent. of phenol. The resulting solution is not irritating to mucous surfaces, even in the presence of active inflammation. R. C. Graves (Jour. of Urol., Dec., 1925).

Pneumopyelography.—This procedure consists in the injection of a gas, usually oxygen, into the renal pelvis for contrast purposes. According to S. A. Thompson it gives greater contrasts than the opaque solutions. Any excess of the oxygen flows back outside the catheter in the ureter down into the bladder, distending the wall along the way.

Perirenal Inflation.—Perirenal inflation was introduced by Carelli and Sordelli, of Buenos Aires, as an improvement over artificial pneumoperitoneum in X-ray demonstration of the kidney where simple X-ray examination proves unsatisfactory.

A long platinum needle is introduced, perpendicularly, to the transverse process of the second lumbar vertebra, then slightly deviated to graze the bone; when the manometer shows oscillations, the needle is known to be in the perirenal fatty tissue, and from 200 to 500 c.c. of carbon dioxide gas is then introduced and an X-ray picture at once taken. The gas is soon absorbed and the discomfort passes off. The kidney

stands out plainly like an island in a lake of air. The method, though serviceable, may, perhaps, be lacking in safety, as instances of mediastinal and cervical emphysema, puncture into the peritoneal cavity, and signs of embolism have been reported.

ANOMALIES OF FORM AND POSITION.

Absence.—*Absence of both kidneys* is incompatible with life, but *congenital absence of one kidney* is not. In the latter case the organ missing is usually the left; the remaining organ may be supplied with two pelves and two ureters. The absence of a kidney may be suspected when dullness over the normal site of the kidney is replaced by a tympanitic note. Serious results from the anomaly are only to be anticipated when the remaining kidney becomes diseased.

Lobulated Kidney.—This is the most frequent form of anomaly, and is really a *perpetuation of the fetal lobulation of the organ*. The fissures are sometimes sufficiently deep to divide the organ into several reniculi.

Horseshoe Kidney.—From the surgical viewpoint this is the most striking of anomalies. It usually consists in a union of the lower ends of the two organs by means of renal or fibrous tissue. At times the middle segments of the organs are found united, and, rarely, their upper ends. A horseshoe kidney is usually located immediately above the promontory of the sacrum, but it may descend deeper into the pelvis on either side of the spinal column. In most cases, however, especially in very thin persons, it is recognized above the sacrum.

Among 36 cases of gross renal and ureteral anomalies observed in the Mayo Clinic in 5 years, 12 were of the horseshoe type. Usually the fusion consisted of renal tissue and varied from

a small area to the full width and thickness of the kidney. Ninety per cent. of cases were fused in front of the great vessels. C. H. Mayo (N. Y. Med. Jour., Mar. 1, 1913).

According to Rovsing, the presence of horseshoe kidney should be suspected whenever a patient complains of an oppressive pain across the abdomen from one kidney region to the other which subsides completely when the patient assumes the recumbent position. The pain is accentuated by physical exercise and when the spine is bent backward, when the patient stands. A tumor can often be detected on the left or right side of the spine immediately above the sacral border. Hydronephrosis is a frequent complication of horseshoe kidney.

The most common disease affecting horseshoe kidney, found in 649 cases, is hydronephrosis, which later may become pyonephrosis. This hydronephrosis is apt to occur in moderately young individuals, while pyonephrosis and lithiasis are usually seen in middle-aged subjects or later. Tuberculosis is rarely witnessed. C. H. Mayo (N. Y. Med. Jour., Mar. 1, 1913).

Treatment.—The treatment of horseshoe kidney consists in separating the organs, *i.e.*, division of the isthmus. When the organs are diseased, measures appropriate to the condition present must be instituted. Either one of the operations described later in this article may be indicated, where the malformed or united organs give rise to morbid symptoms.

Besides 3 personal cases of horseshoe kidney with hydronephrosis in 2 of them, the writers found 9 operative cases on record of hydronephrosis with horseshoe kidney with operative treatment and 15 cases in which the trouble was first noted at necropsy. **Heminephrectomy** in 9 operative

cases was successful in all but 1; in this the fact that the kidney was of the horseshoe type was not recognized until the attempt had been made to remove the whole kidney mass. Fatal hemorrhage followed from laceration of a large vessel. Papin and Christian (Annales des mal. des org. g nito-urin., Oct. 15, 1910).

When the writers do not have absolute data as to the condition of both kidneys, they always explore the other kidney, usually through a separate incision, before the removal of a tumor of the kidney or the removal of a diseased kidney. In abdominal surgery, where the type of the presenting tumor is questionable, the kidney should be palpated before removal of the tumor. In some instances transperitoneal incision is indicated. C. H. and W. J. Mayo (N. Y. Med. Jour., Mar. 1, 1913).

MOVABLE AND FLOATING KIDNEY.

The term *movable* kidney is used to designate those cases of displaced and not fixed kidney in which the movements are entirely subperitoneal. In *floating* kidney the movements are intra-abdominal; the organ is surrounded by peritoneum and has more or less of a mesonephron. The former variety is usually acquired, while the latter is said to be only congenital. This, however, is quite doubtful.

SYMPTOMS.—The subjective signs of movable kidney range from slight discomfort to intense pain, Dietl's crisis, depending, to some extent, on the amount of mobility. Most commonly the pain is dull, aching, or dragging, located in the loin and aggravated by exertion, constipation, and often by menstruation. Occasionally it is paroxysmal, not unlike renal colic. Kinking or torsion of the ureter may cause transitory at-

tacks of hydronephrosis. Gastric symptoms and disorders of digestion have also been frequently observed.

[Edebohls reported 58 cases in which he believed appendicitis was caused by the venous stasis in the region of the cecum resulting from the pressure of floating kidney. This view seems confirmed by the relief of symptoms in 12 cases by nephropexy. W. W. KEEN AND M. B. TINKER.]

On palpation, a tumor of the size, form, and consistency of the kidney can be usually made out; the tumor slips away under the fingers, generally to the region of the loin. The range of mobility may be slight, but in some cases it is so great that the tumor may be felt near or past the median line or in the inguinal region. Manipulation often gives rise to sickening pain, similar to that produced by compression of the testicle or ovary.

According to Cheyne, movable kidney is, in part at least, a congenital defect. As to its appearance suddenly under trauma or strain, Cheyne suspected that in many cases the organ had been movable beforehand without symptoms. The symptoms occur in 3 groups: The first group consists of indefinite symptoms, giddiness, faintness, anemia, palpitation, neurasthenia, etc., and particularly neuralgia; the second group consists of those due to involvement of the intestinal tract, reflexly or by pressure; the third consists of those due to twisting or obstruction of the pedicle. Clarke noted that in the acute attacks great intestinal distention was usually present. Rolando points out that the pain induced by movable kidney may be mistakenly ascribed to the appendix. Morris emphasizes abdominal rigidity as diagnostic evidence that a movable kidney is a factor in nephritis, gastric hyperacidity or congestive appendicitis.

When the pedicle of the kidney becomes twisted or kinked, there may be, if obstruction is limited to the renal vein, merely a dull pain. Dietl's crisis, with more severe pain, occurs where the obstruction involves the ureter. The pain radiates along the

ureter and in the lumbar region, may be referred to the opposite side, and may be attended with nausea and vomiting, fever, and even collapse. Local or more extensive tenderness may be present. Such attacks are associated with a process of hydronephrosis, and last from a few hours to 2 days, terminating with a temporary polyuria, which succeeds the diminished output or actual reflex anuria generally present during the attack.

Hematuria may occur either in conjunction with or apart from Dietl's crises; it suggests that dilatation of the pelvis is taking place and indicates operative treatment.

Roentgen ray diagnosis may be brought into use by injecting an opaque medium into the renal pelvis and making X-ray plates with the patient in various positions. That the patient's pains are actually due to the kidney may be ascertained by injecting a sterile solution into the renal pelvis, using a large ureteral catheter to prevent back-flow, and noting whether an exact reproduction of the pain is awakened in this manner.

The diagnosis from very mobile, distended gall-bladder and tumors of the intestine, especially the large intestine, is sometimes difficult. The kidney is much more deeply located posteriorly, however, and if it is possible to fix the liver it will be impossible to make the gall-bladder disappear as the kidney does.

Percussion over the back shows clearly that the normal bed of the kidney is empty. Even in the cadaver the writer was often able to determine the outlines of the kidney with great precision. Galdi (*Riforma medica*, Oct. 23, 1920).

In the case of intestinal tumors stenosis of the gut sometimes settles the diagnosis. This can readily be established by X-ray examination after an opaque meal. Tumors of the omentum occupying the right hypochondrium are rare, growths of the pylorus usually cause greater gastric disturbance and are situated higher

and nearer the median line, and impacted feces disappear after a purge.

ETIOLOGY.—The condition is much more common in women; it is most frequent during the child-bearing period and particularly in women who have borne several children. This is thought to be because of the lax condition of the peritoneum and of the abdominal wall, and the absorption of the circumrenal fat thus induced, for movable kidney may follow emaciation due to any wasting disease. The right kidney is affected four times as often as the left; this is attributed to the proximity of the liver, which, in its movement downward with the diaphragm, may force the kidney before it. Traumatism has been mentioned as a cause, but this is not in accord with the infrequency of the condition among males. Probably in most cases renal mobility is to be attributed to a combination of several causes, and accompanies general enteroptosis of greater or less degree.

Case of dystocia due to prolapse of a floating kidney into the pelvis in front of the pregnant uterus. The patient was a primipara aged 21. She gave a history of attacks of acute pain in the right side, followed frequently by the passage of a large quantity of pale urine. After 3 hours of hard second-stage pains, the head was well engaged at the brim. The concavity of the sacrum was occupied by a mass of the shape, size, and consistency of the right kidney. The kidney was freely movable, and during examination was forced up over the brim of the pelvis. The woman was then delivered by forceps. Immediately and a few days later, the kidney could be made out freely movable in the right abdomen and replaceable. The baby was born alive and well. Willson (Wash. Med. Annals, Jan., 1911).

TREATMENT.—In a few cases the application of a suitable abdominal support is all that is necessary.

Where the abdomen is flaccid some means of support, as **bandages** or a **corset**, should be employed and will be found sufficient in the majority of uncomplicated cases. They must, however, exert pressure upon the entire abdomen from below upward and from above backward, and lift the kidney indirectly, that is, through the subjacent abdominal contents. **Rest on the back** temporarily relieves the frequently recurring pains. **Massage**, if employed at all, should be very gentle. Fürbringer (Deut. med. Woch., Nu. 18, 1911).

The writer applies a **belt** that will effectually support the abdominal region, keeps the action of the bowels free, preferably by means of **salines**, because of their action as cholagogues, gives a diet principally of **meat**, and prescribes **sodium bicarbonate**, half a tumbler of **Grande Grille Vichy water** every morning, heated to 104° F. G. Monod (Pract., Nov., 1913).

In Dietl's crises pain may be relieved by draining the pelvis of the kidney with the **ureteral catheter**. **Operation** is indicated in such cases, not only because the attacks will certainly recur, but because pathologic changes in the kidney may be developing. T. E. Hammond (Lancet, Feb. 13, 1926).

If non-surgical measures prove unavailing, operation should be considered if the severity of the symptoms warrants it.

Operative Procedures.—*Nephropexy* or *Nephrorrhaphy*.—By this term is meant the operation for fixation of a movable kidney. The operation was first performed in 1881 by Hahn, of Berlin, who operated upon 2 cases of movable kidney in that year.

Before the introduction of *nephropexy*, *nephrectomy* was performed for the relief of movable kidney; but at

present the latter operation would only be considered justifiable in case of some severe complication, such as strangulation or suppuration.

Extracapsular fixation of the kidney, or **nephropexy**, is surgically feasible, is effective primarily, and comes nearer than any other procedure to restoring the pathologically movable kidney to its normal anatomical relations and to the exercise of its normal physiological functions. C. A. L. Reed (Jour. Amer. Med. Assoc., Sept. 17, 1910).

Technique of Nephropexy.—The patient is placed on the sound side, considerably inclined forward, resting on a hard pillow or pad, so as to increase the costoilic space. The incision for nephropexy answers also for nephrotomy, nephrolithotomy, and nephrectomy. The twelfth rib is carefully located by both palpation and counting, to avoid the possibility of opening the pleura. Beginning $\frac{1}{2}$ inch below the last rib and close to the outer border of the erector spinæ, the incision is carried obliquely downward and forward for about 7 to 8 cm. (3 inches). It divides the skin and subcutaneous tissues, the superficial fascia, the latissimus dorsi, the external oblique, the internal oblique, the transversalis with its aponeurosis, and the deep layer of the lumbar fascia. The anterior border of the quadratus lumborum may require division if impossible to retract it sufficiently. The muscle-splitting method of exposure may be substituted for direct incision in many cases requiring moderate exposure, the advantages being lessened risk of injuring blood-vessels and nerves and of postoperative hernia. With retraction the perinephric fat usually bulges in the wound and is separated prefer-

ably by blunt dissection, exposing the bluish, fibrous capsule. The kidney is pushed well upward and into the loin by the hand of an assistant pressing on the abdominal wall. Special care should be taken that the kidney be in its normal position. The kidney is secured by passing 4 to 6 sutures through the capsule and about 2 cm. (1 inch) of kidney substance and then through the adjacent fascia and muscles of the wound, tying subcutaneously. Fine silk, kangaroo tendon, and chromicized catgut are used as suture material; but if catgut is used, it should be made certain that it is not too readily absorbable.

After the kidney is firmly fastened in place the external wound is closed and the usual aseptic dressing applied.

A movable kidney may induce disturbances of 3 kinds—pain, dyspepsia or nervous instability, or all combined. When pain and dyspepsia occur, the writer keeps the patient in **bed** for several days. Fixation is unnecessary when the displacement of the kidney forms part of a general tendency to ptosis. General **gymnastic exercises** and **hydrotherapy** to strengthen and tone up the abdominal wall are indicated, resting the sagging abdominal wall by **frequent reclining**. This affords a living abdominal band which is better than all artificial measures. A strong and elastic abdominal wall is one of the best means for restoring a sagging kidney to place. An **abdominal band** may usefully supplement this. Treatment for the nervous instability is helpful for the subjective symptoms. Uteau (Prog. méd., Aug. 30, 1919).

Nephropexy is a justifiable operation. It relieves symptoms and is indicated when the belt fails or is poorly tolerated; in cases complicated by ureteral kink caused by fibrous bands; when the sag of the kidney has caused the ureter to kink over an aberrant vessel;

where adhesions have developed around a prolapsed kidney, holding it out of place, and in chronic colon pyelitis when faulty drainage due to increased mobility is not corrected by the belt. The writer employed nephropexy in 30 cases, with success in 96 per cent. Of the 30 cases, 46 per cent. had obtained no relief from mechanical supports used from 6 months to 1 year. He recognizes, however, that a majority of cases of renal ptosis can be relieved by proper **abdominal support, fattening** and strengthening **exercises**. Stress laid, in operation, on exposure of the ureter and relief of any condition present which would defeat the purpose of the operation. C. P. Mathé (Surg., Gyn. and Obst., May, 1925).

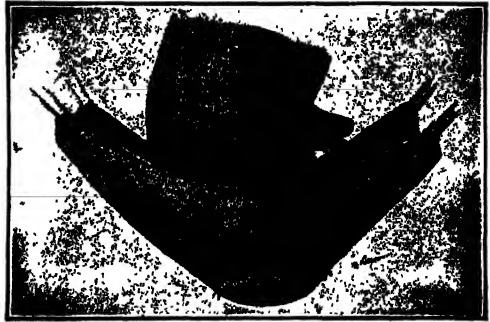
Various modification of this operation have been suggested, having as their main object the securing of firmer or more general adhesions about the kidney.

Packing the wound with gauze, incising and stripping back the capsule so as to get a raw surface in contact with the surrounding parts, splitting the quadratus lumborum longitudinally, dividing its lower attachment and making a muscular sling, may be mentioned among these procedures, but simply stitching the kidney in place, as described, has given satisfactory and permanent results in the experience of several prominent surgeons.

Although the oblique incision is generally recommended, a vertical incision along the sacrolumbalis muscle permits of more ready access for the purpose of securing the kidney in its normal axis.

Hammock operation: The kidney is laid bare by an oblique lumbar incision and brought into the wound by pressure on the abdomen, so that its lower pole can be fixed with the fingers. A strip of fascia lata, from 18 to 20 cm. long, by about 10 cm.

broad, is taken from the thigh, and its four corners secured with artery forceps. An incision about 4 cm. long is made longitudinally in its middle, into which the lower pole of the kidney is introduced, so that the kidney lies in the strip of fascia like a stone in a sling, and is secured in place by sutures passing through the margins of the opening and the capsule. The sling is then fastened in its desired position by sutures. By this means the lower pole can be drawn a little forward, if the upper pole shows a tendency to droop. The advantage of this method of operating is that the



Fascia hammock for wandering kidney. (Kocher.)
(Correspondenzblatt für Schweizer Aerzte.)

kidney is kept in place without depending on any sutures in the kidney itself. T. Kocher (Correspondenzbl. f. Schweizer Aerzte, May 3, 1913).

Experiences in 189 cases of wandering kidneys in which **Rovsing's method** was applied. Decapsulation in connection with suture of the capsule proper is the most reliable procedure, while it makes the least demands on the patient. The kidney is drawn up into the incision; the latter skirts the margin of the erector spinæ, from the tenth rib to 2 cm. below the twelfth, where it turns forward at a sharp angle for 6 or 8 cm. The drawn-up organ is cleared from all adhesions with scrupulous care and the true capsule is incised along the convex margin of the kidney with a short transverse incision at each pole. The capsule is then turned

back on each side, leaving a rectangular opening. A stout silk thread (No. 4 English) is then carried around the lower pole of the kidney, weaving it in and out of the true capsule beyond the area of the incision. This suspends the lower pole as in a sling and the kidney is then restored to place. The ends of the silk are brought out separately each side of the incision in the skin.

When the kidney is thus pushed and drawn up into its normal place, with room for normal play, the patient is turned on his back and is not allowed to get up for four weeks. The threads are removed the third week. In the uncomplicated cases all trouble was permanently at an end after the operation in 85 per cent.; adding to these the improved cases, 95.4 per cent. of the patients were cured or materially benefited. The decapsulation insures adhesions which anchor the kidney firmly in place to the transverse fascia, and not to fat tissue. The parenchyma is left intact. The necropsy in a few cases after death from intercurrent disease and in animals confirmed the reliable outcome. The cases in which symptoms recurred are analyzed, seeking for the cause. One of the patients died from peritonitis, suppuration occurring along the course of the silk. This is the only one of the 4 deaths for which the operation can be held responsible. It suggests that silk impregnated with silver nitrate might be preferable. Scheuermann (*Jour. Amer. Med. Assoc., from Archiv f. klin. Chir., Mar. 24, 1914*).

NEPHROLITHIASIS.—Nephrolithotomy.—The removal of a stone located in the substance, calices, or pelvis of the kidney—is indicated when the diagnosis is reasonably certain. (For the medical treatment see NEPHROLITHIASIS, in the preceding article.)

Technique of Nephrolithotomy.—The preparation of the patient and the incision are the same as for nephropexy.

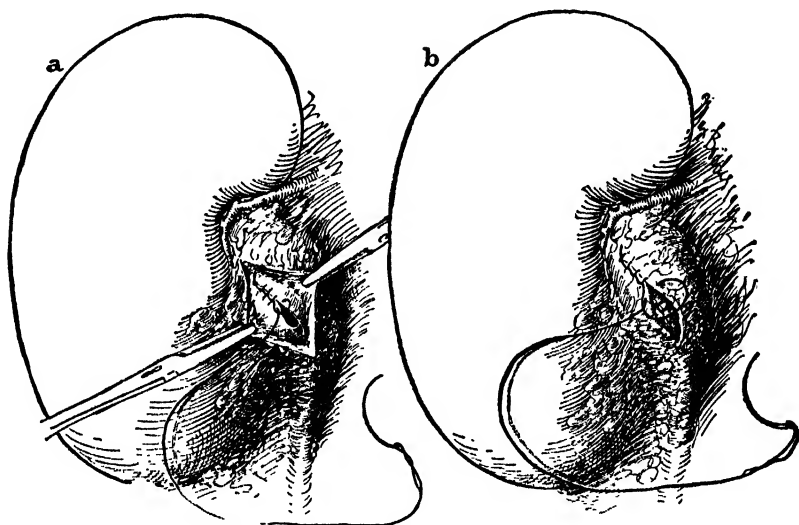
Edebohls's bag, placed under the patient lying on the side, is of much value in bringing the field of operation into prominence. Deep manipulation is facilitated by dividing the last rib, also the outer edge of the quadratus lumborum, or if more room is needed, for inspecting or freeing the kidney or for controlling hemorrhage, the incision may be curved downward and forward toward the abdomen. Free enough exposure to permit delivery of the kidney into the wound greatly facilitates operation. After opening the fatty capsule, the kidney should be systematically examined by pressing on its surfaces or compressing it between the thumb and fingers. Henry Morris recommends that the pelvis and upper end of the ureter be palpated before the kidney is disturbed in order to detect any small calculus that might be present and prevent its falling into the ureter during manipulation. If no hard spot is detected after the entire kidney has been squeezed between the fingers, some operators recommend that exploratory punctures be made from one end of the kidney to the other with a fine needle. This procedure is to be condemned as most unreliable for diagnostic purposes.

In case a stone is found the kidney must be opened, and if none be found the same procedure is necessary for thorough exploration. In either case an incision should be made in the border, in the non-vascular line first mentioned by Hyrtl and recently further emphasized by Brödel's exhaustive studies. Hemorrhage is controlled by compression of the pedicle by assistant and at the close of the exploration by catgut sutures through the kidney substance. Large calculi,

particularly if branched, often have to be broken with forceps before it is possible to remove them. Openings in the pelvis sometimes give rise to urinary fistulae; when, therefore, it seems feasible, it is best to extract through an opening into renal tissue.

Whether a calculus is found or not, the ureter should be catheterized through the pelvis of the kidney from end to end, to determine that it is not obstructed. In calculous pyone-

The writer recommends the use of **distilled water** in large quantities to prevent recurrence of kidney stone and renal colic. For acute renal colic the use of **morphine** and **atropine** hypodermically, followed by the ingestion of 2-ounce (62 Gm). doses of **glycerin** with large quantities of distilled water, has seemed to be of value in aiding the discharge of the stones spontaneously, especially when the patient was in a very hot bath. Ochsner (Jour. Amer. Med. Assoc., lxxiii, 1105, 1919).



a, Pelvis of a kidney which has been laid open for the extraction of a stone, half closed with a running locking suture of chromicized gut. The fascial layer spoken of in the text is the one drawn aside by the forceps. *b*, chromicized gut or fine black silk suture closing the fascial layer over the line of suturing in the renal pelvis proper. This fascial layer is a little too distinctly defined. (Kelly)

phrosis free drainage is necessary, but in most cases the kidney wound is sutured with buried catgut. The wound is closed, leaving a small drain, and dressed with the usual aseptic precautions.

Probably no major operation has a lower mortality, particularly if undertaken early, before any serious renal changes have resulted.

Cellulitis, renal fistula, and renal abscess have been mentioned as possible consequences of the operation.

Thorough flushing of the urinary channels by **drinking freely of water**, preferably distilled water, may help in the dislodgment and removal of any possible nucleus of future stones. This treatment must be continued a long time, even after the urine has completely cleared up. Leaving fragments of stones at operation may favor recurrence. Lamson (Annals of Surg., lxxxi, 16, 1920).

TUMORS OF THE KIDNEY.

The greater number of tumors of the kidney are malignant. Sarcoma, however, is much the most common

form; carcinoma comes next in order; adenoma is not uncommon and is said to degenerate frequently by epithelial overgrowth into carcinoma; fibroma, lipoma, angioma, myxoma, and tumors of the adrenal are more rarely observed.

Study of early diagnosis of kidney tumors in 265 articles in the literature on the diagnosis of kidney disturbances. None of the modern methods of investigation has equaled in diagnostic importance the classic triad, pain, hematuria, and tumefaction, but many tumors in the kidney run a latent course. In adults hematuria is generally the earliest symptom, but it is rare in children. The bleeding usually continues through the entire micturition; it may begin without apparent cause or pain or may follow palpation or jar from any cause, driving or running. Blood-stained urine may alternate with normal urine. Generally the hematuria is of brief duration. Cystoscopy is important, as even with a palpable tumor the blood may come from the other kidney. The pain with a kidney tumor is described as a dull ache, coming on spontaneously and not influenced by repose or exercise, as a rule. It may radiate from the lumbar region to the liver, abdominal walls, bladder, anus, testicles, or vulva, or into the hips, thighs, shoulders, or breast, in the latter case suggesting intercostal neuralgia, or there may be reflex pain in the other kidney. Pasteau has called attention to some new remote tender points in kidney disease. They are along the course of nerves which issue from the spinal cord at the same point as those which innervate the kidneys. Israel found fever a pathognomonic and sometimes the only symptom of cancer of the kidneys or adrenals free from febrile complications. This was the case in 8.2 per cent. of 146 cases. Röntgenoscopy is of not much use in diagnosis of kidney tumors. The absence of cachexia with a kidney tumor of long standing suggests that it

is a hypernephroma. P. Frangenheim (Centralbl. f. d. Grenzgeb. d. Med. u. Chir., May 23, 1912).

Cysts.—Various forms of cysts: simple serous, usually single but sometimes multiple; hydatid cysts; dermoid cysts; and polycystic degeneration, are frequently seen.

The prognosis, according to the writer, is notoriously bad in malignant tumors of the kidney, and the most distressing feature is that it bears little relation to the size and duration of the growth. A very small hypernephroma may invade the vessels and metastasize very early, while a very large one may not metastasize at all. S. Stillman (Calif. State Jour. Med., xv, 363, 1917).

Polycystic degeneration of the kidneys is in almost all instances a bilateral affection. In cases in which, for the time being, one kidney appears to be anatomically and functionally healthy an involvement of this organ may be expected to develop later. Determination of the kidney function is indispensable prior to decision upon any operative procedure. Nephrectomy in cystic kidney is always contraindicated. Excruciating pain, general sepsis caused by suppurations of cysts, profuse hematuria, and distressing symptoms due to the presence of enormously large cysts are, under favorable conditions (good renal function), indications for operative interference. **Nephrotomy with puncture** of cysts, **decapsulation**, and **nephrofixation** are the operative procedures which in selected cases may give satisfactory (temporary) results. Kroloszyner (Amer. Jour. Med. Sci., Sept., 1909).

The diagnosis of infected cystic kidney is generally very difficult, as the physician seldom thinks of the possibility of this rare condition. It is peculiarly liable to become infected. Sieber found infection mentioned in 10 per cent. of 200 cases on record, and Borelius in 1 of his 4 cases. Bull calls attention to the family tendency

in his cases. **Nephrectomy** was done in 61 cases, with 20 fatalities; 8 of the patients were still living after 3 to 7 years. Bull (Norsk Mag. f. Lægevid., Aug., 1910).

Out of 25 nephrectomized cases of polycystic kidneys with suppuration, 16 recovered. In the writer's 4 cases, **flushing out the renal pelvis** restored 1 patient to active life on 2 occasions. Chevassu (Jour. d'urol., May-June, 1921).

In 4 out of 6 cases of bilateral polycystic kidneys, the condition was painless, but in 1 there were several attacks of acute pain with nausea and vomiting. In 1 case the liver was also polycystic. In all cases the left kidney escaped palpation, pushing up the diaphragm, and its condition was determined only by fluoroscopy. Abstinence from operation advised unless complications require it. Out of 128 cases treated by **nephrectomy**, 38 died, 32 were cured, and the outcome was uncertain in 56. S. Rolando (Jour. d'urol., Feb., 1922).

Decapsulation of a polycystic kidney carried out in 3 cases, with good results. The cysts are opened with scissors, the cyst wall resected, and the cystic tissue peeled from the surface of the kidney. The procedure was carried out to relieve pain or hematuria, and in 1 case was practised on both kidneys, at 4 years' interval. Marion (Jour. d'urol., Apr., 1922).

Case in a girl of 3 years in which a single **blood transfusion** caused remarkable improvement, though the child ultimately died of uremia. C. H. Greene (Amer. Jour. Dis. of Childr., July, 1922).

The writer brings a polycystic kidney to the surface to be treated by **ignipuncture**. With the galvanocautery he pierces each cyst, or makes a crucial incision with it in the cyst, or cuts out the presenting portion by running the cautery around it. All of 5 cases were benefited, and all are in good condition except 1 patient who succumbed to the progress of a duodenal cancer. Payr (Zeit. f. urol. Chir., Mar. 29, 1923).

Sarcoma is by far most frequently met with in children and is usually congenital. The tumor is generally of the round or spindle-celled variety, highly malignant, of rapid growth, and often attains enormous dimensions.

Case of sarcoma of kidney, at least 10 cm. in diameter, in a child of 14 months, in which 2 tubes of **radium** were buried in the tumor through a laparotomy and left for 24 hours. In 2 weeks not a trace of the tumor could be palpated. After 3 months it became manifest again, but smaller, and subsided anew under radium. At 22 months the child weighed 11,760 Gm. (26 pounds). Two **X-ray** treatments had also been given. Foster and Mendilaharsu (Sem. méd., Oct. 8, 1925).

Carcinoma is said to result in some cases from traumatic irritation, as from calculi, or to follow inflammatory processes. As a rule, the tumor is of slow growth, and the neighboring lymphatic glands are not affected until late. Extension of the disease to surrounding organs is not common and metastases are still more rare. All these factors favor the success of the operation. If a malignant growth be large and of some months' standing, however, particularly if it is adherent, operation is contraindicated.

In renal *papillomata*, implants occur from above downward or in the direction of the urinary stream, and never from below upward unless by continuity. Implants may occur anywhere along the ureter, but especially where there is a retarded flow, as at the vesical orifice, or at points of injury, as when the ureter is severed and tied on partial removal. In **operating** in this condition, it is best to remove the ureter *in toto*, preferably by the combined transperitoneal and transvesical route. Bissell (Surg., Gyn. and Obst., Mar., 1925).

SYMPTOMS.—Renal growths frequently give no symptoms, remaining latent for some time. Tumor, pain, and hematuria are most important symptoms. The tumor is situated in the loin, growing anteriorly; is smooth and rounded, resists movement on pressure, and does not descend on inspiration. Pain is quite a constant symptom in adults. It is usually dull, aching, felt chiefly in the loin, but may be lancinating, radiating to the scapula and back and to the thigh. Hematuria may be the first symptom, particularly in case of sarcoma, and is irregularly intermittent. Carcinomatous tumors are apt to be nodulated instead of smooth and rounded, as are most renal tumors. In advanced stages fragments of carcinomatous tissue may be passed in the urine. The patient becomes emaciated and cachectic. Hepatic and splenic enlargements are most apt to be confounded with renal tumors.

DIAGNOSIS.—The differential diagnosis is facilitated by noting the resonance of the colon, which crosses the kidneys, but not the spleen or liver. This is assisted by the detection of the notched edge of the spleen or well-defined edge of the liver, and of dullness on percussion over the flanks. Soft, elastic sarcomata may be mistaken for hydro-nephrosis.

Hypernephroma is commonest between the ages of 50 and 70 and is of comparatively slow growth. *Sarcoma* is more common in childhood and forms a rapidly growing tumor with early cachexia. *Carcinoma* is a disease of later life, gives rise to more pain, and usually to constant hematuria, whereas in sarcoma hematuria may be absent, and in hypernephroma is usually of an intermittent type. Glandular enlargement is more common in carcinoma,

either about the kidney or in distant glands, whereas a pulmonary or osseous deposit is more usual with hypernephroma. R. H. J. Swan (*Lancet*, Feb. 8, 1913).

Study of 32 cases of *hypernephroma* of the kidney. The commonest age was 50 to 60 years; the youngest patient was 37 and the oldest 67. It occurred twice as often in men as in women. The average time from initial symptom to operation was 3½ years. Gross hematuria occurred in 81 per cent.; microscopic hematuria in 94 per cent.; it was the initial symptom in 68 per cent. The initial hematuria commonly followed over-exertion; it was usually profuse, intermittent and irregular. Pain was present in 91 per cent.; renal colic, in 66 per cent.—the latter less severe than in stone and usually with worm-like clots. Dysuria and urinary retention occurred in 25 per cent.; frequency of urination, 12 per cent. A tumor was palpated in 80 per cent., and constitutional symptoms (weakness, malaise, dyspnea and loss of weight) were present in 60 per cent. A temperature of 99° F. or above occurred in 75 per cent. There was diminished phthalein secretion on the affected side. All the cases were **operated**. Six died at or soon after operation; 4 died in 1 to 3 years; 8 were known to be living after 8 months to 9 years, and 14 could not be traced. Among the diagnostic helps are unilateral hematuria on cystoscopy and a distorted renal pelvis on pyelography. M. Cutler (*Johns Hopk. Hosp. Bull.*, July, 1924).

GENERAL SURGERY OF THE KIDNEYS.

When operative procedures are about to be performed on the kidney, the fact that it is occasionally the seat of anomalies should be borne in mind. It may occupy an abnormal position; under such circumstances it will usually be found below and nearer the middle line than usual. It may even be found as low as within the pelvic

cavity. Irregularities of size and shape may also be found, due to abnormal or arrested development.

Sometimes the extremities fuse, forming "horseshoe kidney," or one kidney may be absent, in which case the other is apt to be of unusual size, as we have seen. Again, cases of congenital occlusion of the ureter have been reported, in which it was, of course, impossible for the kidney to fulfill its function.

RENAL DECAPSULATION.—

The proposal to treat chronic Bright's disease by operation was first made by Edebohls (Medical Record, Dec. 21, 1901), who described the operation as follows: The patient is placed prone upon the table, with the author's kidney air-cushion underlying and supporting the abdomen. Both kidneys are thus rendered accessible to operation without the necessity of changing the patient's position. An incision is carried from the twelfth rib to the crest of the ilium along the outer margin of the erector spinæ, without opening the sheath of that muscle. The fibers of the latissimus dorsi muscle are bluntly separated in the direction of their course, without cutting. The iliohypogastric nerve is sought for and drawn to one side or other, out of the way of harm. Division of the transversalis fascia exposes the perirenal fat. This is divided over the convexity of the kidney until the capsule proper is reached. The fatty capsule is now bluntly separated everywhere from the capsule proper, the dissection advancing on either aspect and around both poles of the kidney until the pelvis of the kidney is reached. Now and then the fatty capsule may be found so thickened and adherent,

as the result of chronic perinephritis, that the scissors or knife may be required to separate it from the capsule proper. The kidney with its capsule proper is next lifted from its fatty capsule bed, and if possible delivered through the wound. The capsule proper is divided on a director along the entire length of the convex external border of the kidney, and clean around the extremity of either pole. Each half of the capsule proper is in turn stripped from the kidney and reflected toward the pelvis until the entire surface of the kidney lies raw and denuded before the operator. In separating the capsule proper from the kidney, care must be exercised not to break or tear away parts of the kidney, which is often both very friable and very firmly connected with its capsule proper. The stripped-off capsule proper is next cut away entirely, close to its junction with the pelvis of the kidney, and removed. Delivery of the kidney makes this otherwise difficult work easy. If the kidney cannot be delivered, the capsule proper must be entirely peeled off the kidney by the fingers in the bottom of the wound, and excised as far as possible, any remaining portion being simply reflected backward around the root of the kidney, where it will curl up and stay. The kidney is dropped back into its fatty bed and the external incision is closed.

The results obtained by the various observers who have tried the operation, its indications and contraindications have been reviewed in the article on BRIGHT'S DISEASE, Vol. II. In the experience of many competent surgeons, however, the operation has not given the results expected and it has been abandoned by many of them.

NEPHROTOMY.

Nephrotomy is an incision into the kidney, and is used for **exploration, removal of stone, relief of nephralgia,** as a preliminary to **plastic operation for hydronephrosis** or **pyonephrosis,** or for the evacuation of **cystic or purulent collections of fluid.**

In place of incision, which is usually accompanied by somewhat free bleeding, Cullen and Derge pass a blunt needle carrying No. 3 silver wire through the substance of the kidney in the non-vascular zone and by gentle seesawing the wire cuts out. Animal experiments show reduction of hemorrhage to less than half by use of this method.

The operation may be indicated in **simple cysts, hydronephrosis, hydatid cysts, pyonephrosis, suppurative nephritis, and tuberculosis of the kidney.**

In all of these conditions pus and blood will be found in the urine. The amount of blood is generally small and the cells are abnormal; the pus, if measured, is apt to vary in amount. Renal cells and the characteristic epithelium of the pelvis of the kidney will also probably be found. In all chronic inflammatory conditions casts and albumin are present in the urine. Elevation of temperature with or without chills, loss of appetite, hectic suppression of urine, and uremia may also exist. There will be more or less pain and tenderness over the region of the kidney, and in pyelonephritis and pyonephrosis there may be considerable swelling, redness, and edema. The symptoms of pyonephrosis are those of hydronephrosis plus those of suppuration.

Cysts.—*Simple cysts* of the kidney begin in the renal cortex and grow

toward the surface without affecting the renal tissue, unless they grow to great size, when they may cause pressure atrophy. They are thin-walled, globular, and of varying size, and they contain a pale, straw-colored, albuminous fluid of low specific gravity. They sometimes contain cholesterolin or blood, and rarely the contents are thick and jelly-like. They usually cause no symptoms except those of a growing cystic tumor in the loin.

Hydatid cysts are found more frequently in the kidney than in any other organ except the liver, but are six times less frequent than in that organ. They are usually situated in the secreting substance and tend to rupture into the pelvis without reaching great size. Thinning and atrophy may result, however, from pressure. They may be secondary to hydatid disease of other organs.

In some cases a tumor may be felt on palpation, and fluctuation may be perceptible; hydatid fremitus, as observed in other organs, is rare. If the cyst ruptures into the renal pelvis, the passage of vesicles through the ureter gives rise to symptoms of renal colic. The presence of vesicles and hooklets in the urine would confirm the diagnosis. Blood and pus may also escape with the hydatids.

Hydronephrosis is a distention of the kidney with fluid, caused by an obstruction to the outflow of urine.

A tumor, rounded or lobulated in form and often fluctuating, may usually be felt in the lumbar region. In case this tumor diminishes in size or disappears at times, especially if the diminution or disappearance is accompanied by a profuse flow of urine of low specific gravity, the diagnosis

is almost certain. Severe cases may be accompanied with suppression of urine, and, in case both kidneys are affected, uremia will occur sooner or later. Pain is a variable symptom; it is influenced by the tension and may be wanting.

Its causes are congenital or acquired. Nearly one-third of all cases are said to be due to some abnormal condition of the ureter: impacted calculus, kinks, twists, stenosis, or compression from some abnormality of adjacent structures, such as tumors of the abdominal or pelvic organs. Floating kidney is a frequent cause of kinks of the ureter. Among other unusual causes have been mentioned enlarged prostate, phimosis, and retroflexion of the uterus. The fluid within the cyst is never pure urine, frequently containing neither urea nor uric acid: it is usually a clear fluid of low specific gravity containing chlorides and albumin; sometimes it is brownish from the presence of blood; it may be putrid and ammoniacal; rarely it is thick and jelly-like.

Pyelitis and pyelonephritis both occur most frequently as the result of secondary infection from some disease lower down in the genitourinary tract. If the infection is confined to the pelvis of the kidney it is known as pyelitis; if the kidney substance is affected, pyelonephritis, and in its typical form it is usually called "surgical kidney." Both kidneys are generally affected, and gonorrhea is the ordinary cause of the infection. Calculus is also a very common cause of these conditions, or a calculus may form as a result of the inflammation.

Pyonephrosis.—The suppurative processes in a case of pyelonephritis may go on until the greater part of

the kidney substance is destroyed and only a sack filled with pus remains; this condition is known as pyonephrosis. An after-development of supuration in hydronephrosis produces the same result. (See also article on KIDNEYS, DISEASES OF.)

Renal abscess may result from traumatism, renal calculus, or it may be pyemic or metastatic in origin. Abscesses of the kidney are located in the cortical substance. They frequently empty through the pelvis of the kidney or they may rupture the capsule, giving rise to a perinephritic abscess in the surrounding cellular tissue. In case there are several abscesses the septa between them may break through, giving rise to pyonephrosis. (See also article on KIDNEYS, DISEASES OF.)

Tuberculosis of the kidney is, in the majority of cases, associated with tuberculosis in other organs. The kidney is enlarged, sometimes very considerably, and cheesy masses are seen in the secreting substance. (See also article on KIDNEYS, DISEASES OF.)

Perinephric abscess in most cases results from the extension of suppurative processes in the kidney itself, but it may follow traumatism with or without recognizable injury to the kidney; it may be metastatic in origin following typhoid fever, grip, measles, or peripheral suppurations, or it may result from operative intervention or inflammatory processes in neighboring organs. Not seldom it arises from a local infection of the perinephric tissues.

The abscess tends to burrow along the sheaths of muscles and under the fasciæ of the lumbar region, usually reaching the surface, but sometimes following the sheath of the psoas to

the inguinal region, or finding its way through the diaphragm or rarely bursting through the peritoneum.

The symptoms are those of deep-seated suppuration in this region, but the condition is apt to be of particular gravity because of the debilitated condition of the patient from the previous renal suppuration and the highly poisonous character of the mixed pus and urine. The diagnosis may be confirmed by the use of an aspirating needle. (See also article on KIDNEYS, DISEASES OF.)

TREATMENT.—In any of the above conditions the operation may be indicated. Small *cysts* are frequently found in granular kidneys, however, which never demand surgical treatment, and in case pathological changes are far advanced in any of these conditions the operations of **resection** or **nephrectomy** may offer the patient the best chance of recovery. **Puncture of the kidney** and **aspiration** of the contained fluid is recommended by some surgeons in the treatment of *cysts* and *hydronephrosis*, but, if successful, the procedure has to be frequently repeated in most cases and it very often fails to produce a cure or gives rise to infection.

The indications are more positive when there is *suppuration* in and around the kidney; **incision, evacuation of the pus, and drainage** are necessary. When the diseased condition has advanced so far as to call for nephrectomy, but in which the strength of the patient is much exhausted, incision and drainage are often followed by such gain in strength and improvement of the patient's general condition as will permit of the successful performance of the more seri-

ous operation at a later date. In *tuberculosis of the kidneys* simple **nephrotomy** with **removal of diseased tissue** may be all that is needed; but **nephrectomy** is often necessary.

Technique.—Before all operations of probable gravity examination of the urine to determine the functional capacity of the kidneys (see NEPHRECTOMY), and if possible the condition of the other kidney should be made. In order to lessen the danger of infection from the micro-organisms which are commonly found, even in healthy kidneys, hexamethylenamine or some of the proprietary drugs of like chemical composition may be administered for several days before the operation.

The usual incision for exposing the kidney (described above) is generally the best. In cases of great enlargement, however, it may be more convenient to make the opening farther forward. In operating for cysts or for hydronephrosis the tissues may be found normal, with the exception of a thinning of the perinephric fat; but in suppurative processes the skin, muscles, and fasciæ are likely to be found vascular and edematous, and the perinephric fat dense and adherent. A sufficient surface is usually denuded to permit of its being brought to or near the level of the skin, where it is sutured after being opened. Any curdy or stringy material which may be found within abscesses should be curetted away, and if there are septa between abscesses they should be broken down. After thorough disinfection of the wound a thick drainage-tube is inserted, the wound is partly closed, and a heavy absorbent dressing applied.

Simple cysts often close primarily,

the cavity of an hydatid cyst usually closes after suppuration, and there are a good proportion of cures following nephrotomy for abscess. After operations for hydronephrosis, *fistulae* are often left that will not close without a **plastic operation** or, in some cases, **nephrectomy**. **Resection** or **nephrectomy** is frequently called for after nephrotomy for tuberculous kidney.

NEPHRECTOMY.

Removal of the kidney may be indicated in cases of **renal tumor**; **severe injuries accompanied by serious hemorrhage, suppuration, or infiltration of urine**; in renal or ureteral fistulae, **diseased movable kidney, tuberculosis of the kidney, hydronephrosis, calculus, cyst, and suppurative processes** in which resection seems unlikely to relieve or cure.

But few well-authenticated cases are on record in which this operation was undertaken for injuries of the kidney. While a successful result may follow without intervention, operation has, no doubt, often been delayed until too late. Severe hemorrhage—as evidenced by bloody urine, acute anemia, and the physical signs of fluid in the abdominal cavity—is an indication for immediate exploratory operation. The same is true in the event of severe secondary hemorrhage, which sometimes occurs as the result of the rupture of a traumatic aneurism. It is often difficult to decide what to do if the bleeding is less copious, but in any case operation should not be deferred until the patient is too weak and anemic. In the less severe cases the lumbar incision will answer; in graver injuries the extraperitoneal incision from the tip of the twelfth rib to the junction of the middle and outer thirds of Poupart's

ligament will give more room and seems more generally applicable; celiotomy is called for in case there are signs of hemorrhage into the abdominal cavity. The ligation of vessels and suturing or the use of the tampon followed by suture may be sufficient in less severe injuries, but nephrectomy is indicated in case a main branch of the renal artery is injured or if there is very extensive laceration and contusion of the renal substance.

The conditions under which nephrectomy is indicated—for *renal calculus, hydronephrosis, tuberculosis, cysts, and suppurative processes*—have already been discussed.

Ureteral fistulae, which usually are due to wounds inflicted during operations on the abdominal or pelvic viscera, may necessitate **nephrectomy**, but the operation seems indicated only in case there is great discomfort or the patient is prevented from following a necessary occupation. In most cases it would probably be possible to perform a **plastic operation** on the ureter or, failing in this, to **implant** the end of the **ureter into the rectum**.

Technique.—As a preliminary to the removal of a kidney measures should be taken to determine as definitely as possible whether another kidney exists and whether it is sound or diseased. Numerous segregators and other devices have been suggested for the purpose of collecting the urine from each kidney separately, many of them depending upon the compression of the ureter by various means, but none of them have proved entirely satisfactory. The catheterization of the ureters (see below, DISEASES OF THE URETERS) is the most certain method

of obtaining separate urines, but much special skill is required for its successful practice.

Among the possibilities for false conclusions resulting from ureteral catheterization may be mentioned plugging of the catheter by a small clot or by pus; reflex anuria from the presence of the catheter in a few cases, or polyuria for a few minutes in most cases, which may resemble the flow from retention; also, the appearance of a few blood-cells from traumatism in the first urine.

Likewise of assistance in many cases are such procedures as pyelography, the phenolsulphonphthalein test, and other renal functional tests. (See GENERAL DIAGNOSIS, at the beginning of the present article.)

In some cases it may seem necessary to lay both kidneys bare by lumbar or abdominal incisions to determine the presence of both kidneys or the extent of disease in them.

The kidney may be removed either through a lumbar or an abdominal incision. Abdominal nephrectomy is usually reserved for those cases in which there is great enlargement of the kidney and for cases of injury in which there is hemorrhage into the peritoneal cavity.

The great point in dealing with the pedicle, according to Bland-Sutton, is to avoid including in the ligature any portion of the kidney pelvis. When, however, the pelvis is greatly dilated, with many vessels spread out over it, all these long vessels should be seized with forceps and tied separately with thin silk.

Nephrectomy does not seem to affect the course of pregnancies later. Hartmann has reported 150 pregnancies in 115 women after nephrectomy, with only 3 deaths; in 2 of the fatal cases the remaining kidney was known to have been diseased. In 3 personal

cases there was no trace of albuminuria during pregnancy. Spire and Boeckel (*Ann. de gyn. et d'obst.*, Mar., 1913).

Rough handling of the kidney during **nephrectomy** for hypernephroma seems to favor metastasis, as shown by the rarity of metastases in untreated hypernephroma and their extreme frequency after operation. To obviate this, the writer exposes the renal vein first, instead of last, and places a provisional ligature about it before delivering the organ. Cure was obtained in 1 case in spite of growth of the tumor into the vena cava through the renal vein. The vena cava is ligated in such cases, and the other renal vein sutured to the stump of the cava if its position so requires. Rehn (*Zeit. f. Urol.*, xix, 38, 1925).

In **nephrectomy** non-absorbable material should not be used for ligation of the ureter, particularly when it is dilated. Case in which a silk ligature worked loose 12 years after the operation and was expelled down the still patent ureter with sharp renal colic. H. W. B. Cairns (*Brit. Jour. of Surg.*, July, 1925).

Among 149 **nephrectomies** performed at Hochenegg's clinic, 38 were for malignant conditions, and of these cases 10 died. Among 111 nephrectomies carried out for various other indications, there were 8 deaths. Stress laid on preliminary thorough examination and functional tests. A. Weiser (*Zeit. f. urol. Chir.*, July 31, 1925).

Case of **nephrectomy** in an infant of 7 months, for hydronephrosis. The kidney had 2 pelves and ureters, the latter uniting before entering the bladder. One ureter left the organ at its upper pole. A. C. Morson (*Brit. Med. Jour.*, Feb. 27, 1926).

The lumbar incision gives better opportunity for the separation of adhesions, it is extraperitoneal, and permits freer drainage of abscesses if necessary without serious danger of peritonitis, and the general mortality is considerably less than after abdominal nephrectomy.

A large proportion of patients in whom **nephrectomy** has been performed for severe lesions die during the first year following operation. The majority of cases of renal tuberculosis in which the remaining kidney is more or less involved succumb before the end of four years. On the other hand, patients operated on for tumor or tuberculosis who survive for four years may be regarded as cured. The presence of slight or moderate signs of pyelitis or pyonephritis in the kidney of a nephrectomized person is of no especial moment, as they are apt to disappear after operation. Kummell (*Arch. f. klin. Chir.*, Bd. ci, Hft. 2, 1914).

The writer reports 250 cases of **nephrectomy** based on the findings in catheterization of the ureters and 187 cases based on the findings of the Ambard ureosecretory index. With the latter below 0.100, the mortality was 3.6 per cent.; above 0.100, the mortality was 10 per cent. With catheterization alone, the mortality was 3.20 per cent.

His experience is in favor of the Ambard index as being a reliable guide alone, especially when it is below 0.100. The higher the constant the greater the risk.

The risk is highest when the nephrectomized kidney has been doing part of the work.

With a constant below 0.100 the disease was invariably restricted to one side. Legueu (*Jour., d'Urol.*, ix, No. 1, 1920).

Lumbar Nephrectomy.—The length and direction of the incision depend to some extent on the condition of the organ to be removed. In case the kidney is of normal size or but slightly enlarged and is not adherent the vertical or oblique incision as described under movable kidney could be used for the removal of an enlarged or adherent kidney. The incision, beginning $\frac{1}{2}$ inch below the last rib near the outer border of the erector

spinæ and continued first downward toward the crest of the ilium, then curving forward to the middle third of Poupart's ligament, gives the necessary exposure for safe operation. Kocher used this form of incision and found it possible through it to examine the other kidney or the under surface of the liver with his hand in the abdominal cavity. After determining that the other kidney is sound he sewed together the opening in the peritoneum and proceeded with the removal of the diseased kidney.

The structures divided and their relations have already been described under movable kidney. It is generally possible to separate the peritoneum from the surface of the kidney and to push it inward. The organ is then freed from its bed and the larger vessels going to the capsule are tied. Dense adhesions are divided by scissors, but in some cases they may cause so much difficulty that it will be easier to enucleate the kidney from its capsule rather than to separate it from the circumrenal fat. After it is freed the organ is luxated from its bed, care being taken not to make much traction on the pedicle; the structures at the hilum are isolated, a strong silk ligature is passed about the vessels by an aneurism needle and tied, the ureter is separately doubly ligated and tied, and the pedicle divided.

If the ureter contains infectious material it may be divided with the thermocautery and pure **carbolic acid** injected, as suggested by Howard Kelly. After the pedicle has been carefully inspected in the wound and all bleeding points have been secured a large drainage-tube is placed in the bottom of the cavity and the

wound is partly closed by deep and superficial sutures.

Abdominal Nephrectomy.—Various incisions have been used: An incision in or near the median line will facilitate the exploration of the alternate kidney in case manual examination seems necessary, while the removal of an adherent kidney would be easier through the lateral incision. After opening the abdominal cavity the kidney is exposed by tearing through the peritoneum forming the outer layer of the mesocolon, as its inner layer contains the vessels which supply the bowel, and their division might give rise to gangrene of the intestine. The freeing of the kidney from its bed and the isolation and ligation of the vessels and ureter are then carried out in much the same manner as in lumbar nephrectomy.

The mortality of nephrectomy varies with condition of the patient and the pathological condition for which the operation is undertaken. The prognosis in operations for malignant disease is grave both as to immediate mortality and permanent cure, but there has been great improvement in results with more accurate methods of determining the functional capacity of the kidney and with improved operative methods and technique. The immediate mortality has been reduced from nearly 70 per cent. in the first decade of renal surgery to 25 per cent. or even less in the experience of some surgeons, at the present; permanent cures of from 2 to 18 years are shown in 34 cases reported by Wagner. The proportion of deaths after operations for tuberculosis of the kidney is also much lower in recent years; probably somewhat better than 10 per cent. in the

hands of experienced surgeons; recent statistics place the mortality at about 25 per cent. in case of traumatic lesions, while with less extensive injuries treated by suture and packing there is probably less than 5 per cent.

RESECTION OF A PART OF THE KIDNEY.—The first partial excision was performed by Czerny in November, 1887, for an angiosarcoma. The operation has been rather rarely resorted to, although there seems to be no doubt that it is a sound surgical procedure in the conservative surgery of the kidney to substitute this operation for total nephrectomy when only a part of the kidney is diseased or has been injured.

Report of a case asserted to be the first on record of **bilateral heminephrectomy** involving the lower portions of double kidneys on both sides of the body. The diagnosis of this anomalous condition had been made by finding 2 ureteral orifices on each side of the bladder and confirmed by the use of opaque catheters and pyelography. The condition requiring operation was non-calculous *infected hydronephrosis* of the lower portions of the kidneys. One set of vessels supplied both portions on both sides. The 2 sides were operated on 2 months apart, and the patient made an uneventful recovery. Eisendrath and Phifer (Jour. of Urol., May, 1925).

Case of partial *calculous pyonephrosis* in which, while the lower pole of the kidney was destroyed, $\frac{1}{2}$ to $\frac{3}{8}$ of the organ was grossly normal and functionally capable. The lower portion of the organ was removed alone by a conservative **resection**. Richter and Zimmermann (Surg., Gyn. and Obst., June, 1925).

Nephropexy, or Nephrorrhaphy, and Nephrolithotomy, being indicated only in special disorders, have been described above under the corresponding headings.

TRANSPLANTATION OF THE KIDNEY.

This operation has been successfully done on animals by several workers in laboratories of experimental surgery. It seems to be possible to transplant the kidney to some other part of an animal's body, but not to transplant from one animal to another of the same species, and still less practical to transplant from one animal to another of different species.

An animal—dog—which has undergone a double nephrectomy and the grafting of both kidneys from another animal can secrete almost normal urine with his new organs and live in good health at least for a few weeks. Carrel (*Jour. of Exper. Med.*, Jan., 1908).

A dog, after having undergone a double nephrectomy and the replantation of one kidney, lived in excellent health for almost two and a half years, and died of an intercurrent disease which was without relation to the operation. The autopsy showed the kidney to be normal. Hence the experiment proves definitely that the extirpation of the kidney in the dog, its perfusion with Locke's solution, the complete interruption of its circulation for fifty minutes, and the suture of its vessels and ureter do not interfere with its functions, even after a long period of time. It indicates finally that from a purely surgical standpoint the grafting of organs is a real possibility. Carrel (*Jour. of Exper. Med.*, Aug., 1911).

By vascular suture the writer was able to remove the dog's kidney and later replace it. The function of such a kidney showed initial overaction, as compared with the normal kidney, followed by balanced action. A single, reimplanted kidney is able to maintain normal life indefinitely. Quinby (*Jour. Exp. Med.*, Apr., 1916).

Out of 28 autotransplantations of a kidney in dogs, 2 were successful. There was increased diuresis and

elimination of chlorides on the denervated side. The ureter contracted normally. Lurz (*Deut. Zeit. f. Chir.*, Dec., 1925).

Study of the effects of diuretics, injected intravenously, on autogenous and homogenous kidney transplants. The functional activity and the secretion of autogenous transplants appeared similar, if not identical, to those of a normal kidney, and the effect of diuretics was the same. Viability and function were maintained indefinitely. With homogenous transplants, *i.e.*, transplants from another animal of the same species, viability and function are only transient. As long as they remain viable they function in a manner similar to autogenous transplants. As a rule, however, the early appearance of albumin, red blood cells and pus denotes marked parenchymatous changes. The homogenous transplant responds to a diuretic in much the same manner as a normal kidney, except that diuresis is not so marked nor so prolonged. J. K. Holloway (*Jour. of Urol.*, Feb., 1926).

DISEASES OF THE URETERS.

Examination of the Ureters.—*Inspection.*—The vesical orifices of the ureters can be seen by cystoscopic examination, but for more extensive examination vaginal or abdominal incision is required. For exposing the vaginal portion of the ureter Kelly makes an incision extending from the vault halfway down through the anterolateral vaginal wall. The posterior pelvic portion and lower abdominal portion are exposed after abdominal incision by drawing the sigmoid flexure toward the right to expose the left ureter, and by lifting the caput coli and drawing it also to the right to expose the right ureter. The abdominal portions are exposed by incising the peritoneum reflected over the ascending or descending colon on the outer side, where there

are no vessels, and then displacing the colon toward the median line. The ureter will often be found adhered to the peritoneum as it is separated from the abdominal wall.

Palpation.—The pelvic portion of the ureter may be palpated through the vagina or rectum. If the internal iliac artery can be located the ureter will be felt as a flat, yielding cord lying behind and close to it in the upper part of its course. In the lower part of its course it is distinguished by its direction, size, consistency, and mobility. In case the ureter is thickened or if it be distended or sensitive from disease, it can be much more readily found, and it may be possible to palpate it in any part of its course.

Catheterization of the ureters was practised by Simon, of Heidelberg, in 1875, but with only qualified success.

It is chiefly through the work of Howard A. Kelly that this most important means of investigation has been simplified and brought into general recognition, and it is not only a means of diagnosing disease of the ureter, but a most valuable aid in determining the exact condition of the renal pelvis or of the kidney, in treating disease of the pelvis of the kidney, and in accurately locating the ureters so that they may be avoided in pelvic or abdominal operations.

A general anesthetic is not necessary unless the patient is very nervous. After having emptied the bladder the woman is placed in the knee-chest position or in the dorsal position with the hips elevated. In case it is necessary to dilate the urethra, its sensitiveness is first dulled by the introduction of a pledget of cotton saturated with cocaine, then a well-lubricated, conical dilator is inserted

with a boring motion until a dilatation of 1 cm. in diameter is reached. A cylindrical speculum provided with an obturator is then introduced, the obturator is withdrawn, and air rushes in and distends the bladder.

Light is directed through the speculum into the bladder by a head-mirror and the speculum is withdrawn a little and moved right or left until the ureteral orifices are brought successively into the field. The orifice usually appears as a little transverse slit, with a slight horseshoe-shaped elevation around it, open on the inner side. Sometimes it appears as a pit or hole in the mucosa or as a rosette with an opening in the center. If the observation is continued a little jet of urine will spurt from the orifice for a second or two.

Various types of cystoscopes carrying small electric lights are preferred by many genitourinary specialists and are most practical for study of ureteral conditions in the male. Some distend the bladder with air, others with some solution, and nearly every active worker in this field has his own special cystoscope introducing some features which he considers essential.

The catheter is passed through the speculum until its point rests in the ureteral slit, and it is pushed gently in and toward the side, stopping at once if the slightest resistance is met. The catheter can be introduced even into the pelvis of the kidney and the renal pelvis can be irrigated. Kelly has used a flexible ureteral catheter tipped with wax, which is softened by olive oil, in the diagnosis of calculus in the pelvis of the kidney. The stone makes scratches on the glistening surface of the dental wax which are readily seen with a hand-lens.

Technique of catheterizing the ureters: The first point to be considered is the necessity of finding the opening of the ureter rapidly. It is this necessity for quick action that makes it imperative to have a regular plan and not to wander aimlessly with the cystoscope in the bladder. Unnecessary movements of that instrument will cause contraction of the bladder, which not only make the work difficult, but also delay the examination and make the patient nervous. The best way is first to look for the region where the ureters are expected to be found, and not for the openings themselves. For this reason we first look for the trigone, which can be recognized by the difference in color which it presents as compared with the rest of the bladder. Having found the base of the trigone and holding the cystoscope in the middle, with the beak pointing down, one should next turn the shaft upon its long axis to the right or to the left. Very soon one comes across the angle of the base of the trigone, and in this angle we find the opening of the ureter. Care must be taken, however, that the cystoscope does not move away from the neck of the bladder, which is situated at the upper end of the visual field, and also to see that the motion of the instrument takes place without any sudden jar. Having thus found one opening, it is now necessary to put the cystoscope in such a position that the catheter can enter easily. The orifice should appear as sharp and as large as possible. The catheter must be so placed as to be vertically above the ureteral opening. This is recognized by the fact that the opening which appears as a slit when looked upon at an oblique angle becomes rounded or oval as soon as the prism is placed in a parallel plane with it. If this precaution is neglected, we run the risk of having the catheter slip over the opening instead of entering it. Most of the failures of students are due to the fact that they do not place the instrument in such a position as to allow the

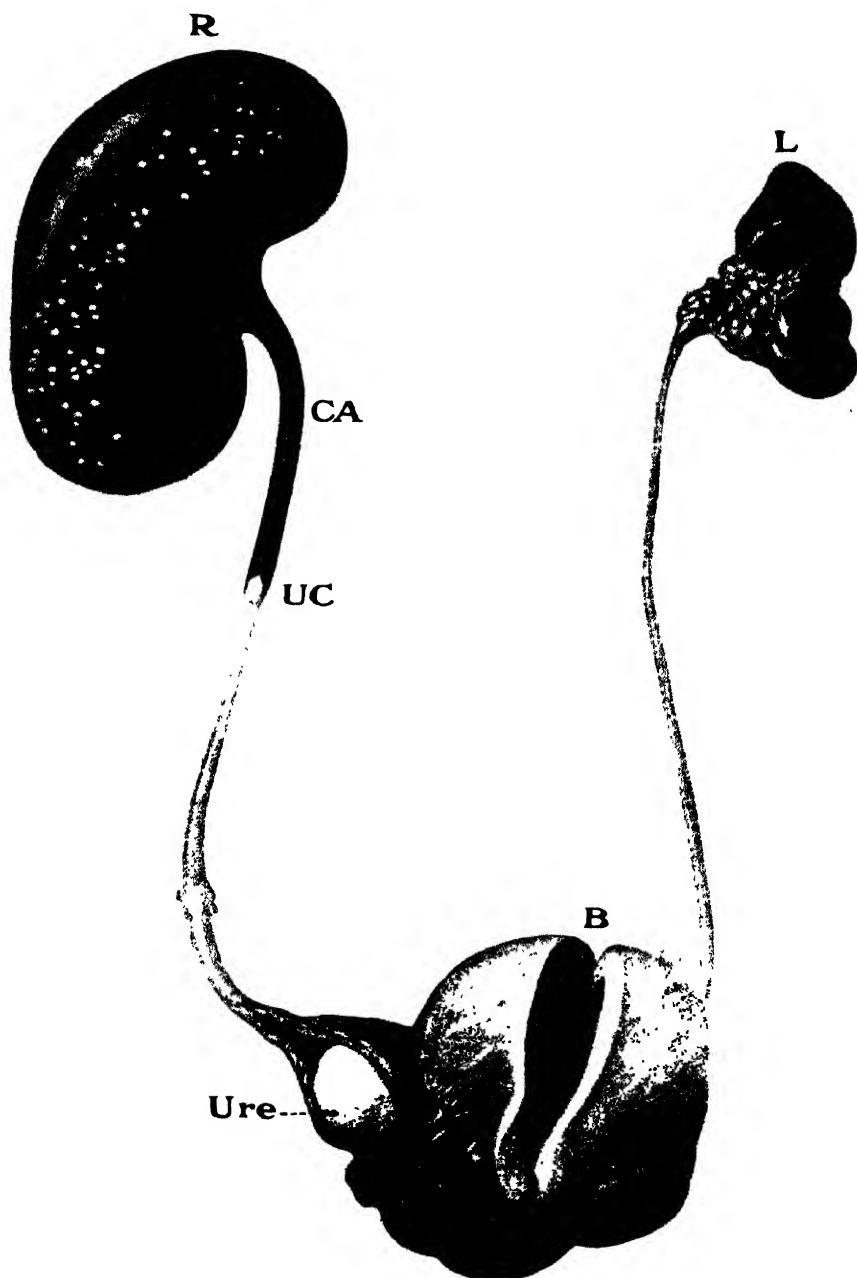
catheter to enter easily. The instrument should be manipulated until the opening appears as large and round as possible, but the movement should be arrested when one finds that deeper shadows are developing in the visual field or that the mucous membrane is becoming indistinct. In this position it is usually easy to enter the opening with the catheter with the aid of the appliances furnished with the cystoscope. H. Loenstein (*Med. Review of Reviews*, from *Med. Klinik*, Apr. 23, 1911).

Palpation of the ureters should be a part of every vaginal examination. Ureteritis, because of the nerves irritated, might simulate disease of any of the abdominal organs. The ureters are marked on the anterior wall by the ureteral ridges, and can be felt from their entrance into the bladder to the pelvic brim. In ureteritis, periureteritis, stone, pyelitis, and tuberculosis, the ureter is thickened and tender. Ureteritis and periureteritis are commonly due to infection from the cervix, and may follow hysterectomy. Palpation shows a thickened tender ureter with intense desire to urinate. Treatment should be applied to the cervix and parametrium and not to the bladder. Tovey (*Amer. Assoc. Obstet. Gynec. and Ab. Surg., Medical Record*, Oct. 30, 1920).

CALCULI IN THE URETER.

These are found most frequently at the junction with the renal pelvis; less commonly about the middle and at the entrance to the bladder.

SYMPTOMS.—Calculi in the ureter usually give rise to attacks of renal colic, whether they simply pass without impaction or become arrested in their course. Impacted calculi are apt to give rise to hydronephrosis, particularly if imbedded near the renal pelvis. At times there is pain or tenderness on pressure at some point in the course of the organ. In the



Specimen Removed at Autopsy, Showing Multiple Calculi in Right Ureter. (*Eisendrath and Herzog.*)

R, greatly enlarged right kidney, showing evidences of suppurative pyelonephritis; *C.I.*, right ureter distended with blood and urine; *UC*, ureteral calculus located just above a stricture of the ureter; *Ure*, large faceted ureteral calculus located in distended vesical end of ureter; *B*, bladder opened in median line; *L*, undeveloped left kidney, showing fetal lobulations.

lower part of the ureter a stone may sometimes be felt by the finger in the rectum or vagina. A positive diagnosis can be made by use of the X-ray or celiotomy and direct palpation.

From a study of 239 cases of ureteral calculi removed by operation or expelled after catheterization (53 cases), Jeanbrau concluded that immediate and complete recovery can be counted on if the patient can bear general or spinal anesthesia and the operation is not done during anuria. A fistula need not be apprehended if the permeability of the ureter throughout its length is determined after extraction of the calculus. The mortality in the cases on record was 1.66 per cent. In examining, after subsidence of the attack of pain, a tender point should be sought along the ureter, above or near the umbilicus, at the intersection of a vertical line passing through McBurney's point and a horizontal line passing through the umbilicus; a second tender point is at the intersection of a line uniting the crests of the ilia and a vertical line through the pubis. The point where the ureter enters the bladder may also be tender.

According to Tenney, 2 symptoms appear in almost every condition which obstructs a ureter. One is pain between the point of obstruction and the 10th rib on the obstructed side. It varies from a dull ache to agony; is sometimes increased by motion, as in stone cases; sometimes brought on by a change from the horizontal to the upright position, as in cases with ureteral kink, and sometimes appears without regard to either, as in purulent or bleeding kidneys, when it comes and goes quickly with the passage of some fibrin mass through the ureter. The other constant symptom consists of increased frequency, urgency, incontinence, or the necessity of repeated attempts before the desire passes away.

Calculi in the lower end of the ureter are manifested above all by vesical symptoms, suggesting cystitis. The cystoscope generally shows a ureteral orifice surrounded by edema. The skiagraph and ureteral catheterization will show with certainty the seat and size of the stone. Pascual (*Jour. d'uroi.*, III, 147, 1913).

The extensive diagnostic field opened by palpation of the ureters in women referred to. It includes calculi and gravel in the ureter, acute and chronic ureteritis and periureteritis, and tuberculosis of the ureter. The writer advises palpation from the lateral vaginal fornix, using left and right index fingers for the corresponding ureters. Judd (*N. Y. Med. Jour.*, cxi, 986, 1920).

A stone in the ureter may long escape detection even though causing constant disturbances. Again, it may remain for years without causing local or general trouble. Radiography, an opaque catheter and pyelography may be required for diagnosis. Sacchi (*Jour. d'uroi.*, July, 1925).

Calculi impacted in the ureter are held in it very often by such conditions as stricture, the size of the calculus, or its rough and crystal-like surface. They often remain in the ureter for years; in the author's series of 60 cases the average time was 9 years. A calculus, once impacted, blocks off the urine, produces pain, pressure, dilatation of the ureter and renal pelvis, keeps up inflammation of the mucous membrane, and in time impairs the function of the kidneys. Such calculi cause intermittent or continuous pain for years, constantly threatening the patient with colic; as a result, the general health is markedly impaired. Stricture of the ureter plays a considerable rôle in the impaction, being found in 18 per cent. of the cases. Contrary to previous teaching, the writer has not found a normal constriction of the ureter except in the lower third, where it travels through the bladder wall. The staphylococcus plays an important rôle in the formation of the stones, having been found in 47.5 per cent. of all the stone cases. Hematuria, microscopic or as red corpuscles, occurred in 94 per cent. of cases. Sixty-seven per cent. of all the impacted calculi were in the lower third of the ureter. The average age of the patient was 43 years. In 96 per cent. the calculi were solitary. Ureteral dilation should be attempted first, as it

was successful in 50 per cent. of the cases. **Extraperitoneal ureterolithotomy** should be performed when dilation has failed. A. H. Peacock (Jour. Amer. Med. Assoc., Dec. 19, 1925).

TREATMENT.—The treatment of calculi passing through the ureter is that already described under renal colic. (See NEPHROLITHIASIS, in the article on KIDNEYS, DISEASES OF, this volume.)

Case of calculus of the ureter in which **glycerin** was used to mobilize the otherwise immobile stone. The author injected 10 c.c. (2½ fluidrams) of sterile, warm glycerin into the ureter. Six hours later the stone was found in the fossa navicularis, from which it was easily removed. Weisz (Berl. klin. Woch., Dec. 4, 1911).

For the **non-operative removal** of stones in the lower pelvic ureter, the writer first manipulates with an **olive-tipped catheter** until the obstruction is overcome. A second catheter is passed an hour later, lubricated, if necessary, with **olive oil** or **glycerin**; **adrenalin** or **procaine** in oil will sometimes overcome spasm. When infection is present, **operation** may be necessary at once, but repeated drainage and introduction of **silver nitrate** solution should overcome such infection. In impassable obstruction, the lower ureter is **dilated** by wedging with a number of catheters. Buerger (Med. Rec., Apr. 1, 1922).

In prolonged attacks of renal colic, with fever and retention of calculi, relief may be afforded by **ureteral catheterization**, as shown in 3 cases described. The catheter, passing, if possible, **over the stone**, at once relieves the pain, and may cause the stone to issue in a few days. Cases were seen in which expulsion of stones occurred in a few days under **bella-donna**, whereas morphine failed. The former drug, given in pills to the amount of 0.08 Gm. (1¼ grains) a day, not only relieves the pain, but also overcomes the spasm of the ureter, without interfering with its peristalsis.

Morphine, while relieving pain, contracts the ureter and impedes descent of the stone. G. Marion (Presse méd., Aug. 5, 1925).

In case of impaction incision into the ureter (ureterotomy) is the only means of relief and cure.

Ureterotomy.—In 1879 T. A. Emmet reported 3 cases in which he had found calculi obstructing the ureter; in one case he removed the stone by forceps after opening the bladder and in another he removed a stone weighing 98 grains by incision through the vaginal wall. Since these operations a very large number of calculi have been removed from various parts of the ureter. Stones impacted in the vesical portion may sometimes be removed with forceps after suprapubic cystotomy has been performed; in other cases a small incision, with careful dilatation of the orifice, will be necessary. From the lower pelvic portion of the ureter stones have been removed by incision through the vagina and through the rectum, but removal through rectal incision is to be condemned because of the danger of infection.

Stones located higher in the pelvic ureter are removed preferably after celiotomy, as the extraperitoneal method requires too extensive denudation. Calculi have been removed from the middle portion of the ureter by both retroperitoneal and intraperitoneal ureterotomy; the retroperitoneal method is the method of choice, exposing the ureter in the way described under **EXAMINATION OF THE URETERS**.

The upper part of the ureter is reached in the same way as the kidney. In some cases in which the stone is lodged high up it may be

possible to push it up into the pelvis of the kidney.

According to Israel, in 64 of 172 reported cases of ureteral calculi the latter were in the pelvic portion of the ureter. Of these, 39 per cent. were palpable by rectum or vaginally. The radiogram was negative in 11.7 per cent. of cases in which a calculus was present. An opaque catheter used in connection with radiography often helps in diagnosis. The operative indications are: Anuria for more than 48 hours; bilateral calculi; retention, with or without infection of the kidney, and acute pyelonephritis. In uncomplicated cases operation depends upon the size of the calculus and the persistence of the pain in a circumscribed area, and is indicated when the calculus has no tendency to descend. For juxtavesical calculi in women a **vaginal ureterotomy** is indicated; in males they may be thrust back toward the kidneys so as to make the incision and suture of the ureter easier. Often calculi can be worked back into the kidney pelvis and a **pyelotomy** performed. In 53 operations performed by Israel there were but 2 deaths, from myocarditis and cardiac paralysis. Twenty-five cases of uncomplicated **ureterotomy** resulted in no deaths.

An X-ray study advised immediately before operation, as stones have a curious habit of passing quietly from the kidney, or up and down the ureter. Stones in the ureter should be given every possible aid to pass on before operation is attempted. Laurie (N. Y. State Jour. of Med., Dec., 1922).

Prompt operation advised. A stone in the ureter can readily be reached by the abdominal extraperitoneal route, through a small incision. The stone can be easily pushed up to allow of readier access, since generally the ureter is dilated above it. E. Leo (Arch. ital. di urol., Jan., 1926).

STRICTURE AND VALVULAR OBSTRUCTION.—The symptoms of this condition are those due to interference with the free flow of urine. Hydronephrosis accompanied by more or less pain is likely to be present; decomposition of the urine, with irri-

tation of the bladder and frequent micturition, is common.

In the cases of ureteral stricture developing large hydronephrosis and hydro-ureter the urologists have been blaming so-called "kinks" in the upper portion of the abdominal ureter. But the ureter is as widely dilated below the kink as above it, pointing to obstruction lower down. Hunner (Surg., Gyn. and Obst., May, 1925).

Treatment.—Kelly has seen great improvement follow **gradual dilatation by graduated hollow bougies** in cases of stricture. **Ureterotomy and division of the valve** or, in case of stricture, **closing the opening after the Heinecke-Mikulicz method of suturing the pylorus**, has been successful in relieving these conditions in a number of cases. **Resection and anastomosis or suturing the ureter into the lower part of the infundibulum** is sometimes necessary.

The opening of the ureter into the bladder is the narrowest part of its course. By means of his **aërocystoscope**, Kelly has been able to pass **graduated bougies** in the course of one or several sittings into the ureteral orifice, and thereby to dilate this up to 6.75 mm. in diameter. For the larger sizes he has used chiefly olive-tipped bougies graduated in thirds of a millimeter. In addition to being of use in the treatment of pyoureter and pyelitis, this procedure can be utilized to obtain the passage of a stone *per vias naturales*, Kelly employing for this purpose an alligator forceps, passed for 5 cm. or more up the dilated ureter to grasp a stone which is out of sight, but which has been previously located by X-rays, sound, or wax-tipped bougie.

The importance of ureteral stricture in the etiology of essential hematuria, frequently with attacks of pain, emphasized. Most of the writer's cases cleared up promptly on **ureteral dilatation with the wax bulb**. Removal of foci of infection is also necessary. Hunner (Jour. Amer. Med. Assoc., Nov. 18, 1922).

SURGERY OF THE URETERS.

While obstetric injury to the ureters is becoming less frequent, owing to earlier interference in difficult cases, gynecological injuries are increasing greatly in frequency, because of the increase of extensive operations—especially the radical operation for carcinoma of the uterus—and also due to the fact that many inexperienced operators are now attempting these difficult operations. Stoeckel asserts emphatically that in all cases, except where a malignant growth is present, it is the fault of the operator if the ureter is injured. It matters not in these cases whether the ureters follow a normal course or are displaced by a tumor, or whether the operation is performed by the abdominal or vaginal route, injury to the ureter is always avoidable if proper precautions are taken. Where a malignant growth is present, however, it is a different story. Here it may be necessary to isolate the ureter for long distances, to dig it out from its carcinomatous bed, to cut through it, or to resect it.

The ureter and the lower pelvis can be exposed by an incision which the writer has used in over a hundred laparotomies. The skin incision runs from the midline about a finger's breadth above the pubes, horizontally outward nearly parallel to Poupart's ligament at first, and curves rather sharply upward at its midpoint to end about opposite the anterosuperior spine of the ilium. This incision is deepened in the same line through the aponeurosis of the external oblique and the internal oblique muscle; the latter is the only structure which suffers any real damage, and only to a slight degree, for the lower part of the incision runs about parallel to its fibers, only the ascending leg cuts across a small part of these fibers.

The incision stops short of the transversalis, which is not disturbed at all. With efficient retraction of the upper flap the external border of the rectus muscle is identified and the fascia of the transversalis is then divided by a vertical incision close to and parallel to the rectus—that is, at right angles to the original incision. Two retractors are then inserted; the outer one retracts the cut edge of the transversalis outward; the other pulls the rectus muscle well toward the midline.

So ample is the space and view that the whole hand can be introduced under the control of the eye. The ureter is released from its surroundings and easily brought to the external level of the wound. In this way it can be handled readily and freely. The wound is closed without drainage. The transversalis fascia is sutured separately with catgut. Continuous sutures of medium-sized catgut (preferably moderately chromicized) are used for the combined internal and external oblique layer. A few interrupted fine catgut sutures are used for the superficial fatty layer. Very fine continuous silk sutures are used for the skin. Gibson (*Amer. Jour. Med. Sci.*, Jan., 1910).

URETERECTOMY.—The term has been applied not only to the total extirpation of the ureter, but to resections of more than 2 or 3 inches of this organ. The operation is indicated in certain cases of tuberculosis of the ureter, hydronephrosis of the ureter, suppuration in a dilated ureter, and in case of lumbar fistula due to the presence of a diseased ureter after nephrectomy has been performed.

The operation may be primary, when the ureter is removed simultaneously with the kidney, or secondary, when the ureter is removed at a subsequent operation. As nephroureterectomy is an extensive operation, usually involving great danger



Fig. 1



Fig. 2.

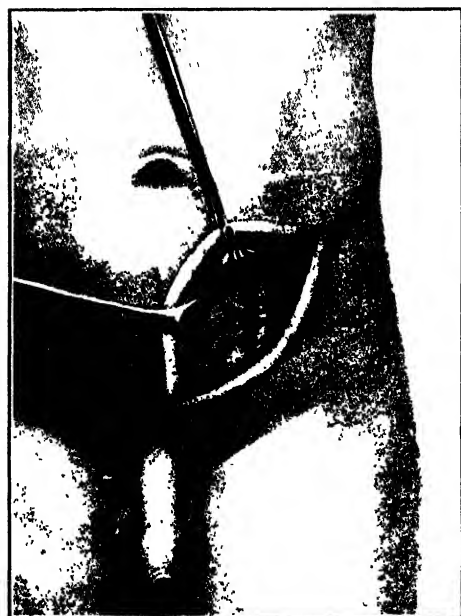


Fig.



Fig. 4.

Technique of Operations on Lower Portion of Ureter. (C. L. Gibson)

Fig. 1, the superficial incision. Fig. 2, the upper flap consisting of skin, external and internal oblique muscles is retracted. The dotted line represents the line of incision in the transversalis fascia. Fig. 3, the edge of the rectus muscle is strongly retracted inward, between it and the cut edge of the transversalis fascia the peritoneum is exposed. Fig. 4, the peritoneum has been pushed upward. The ureter is lifted out of the pelvis and brought to the level of the external wound.

to life, removal of the ureter is frequently performed at a later operation when the patient's condition has improved. The tendency to formation of dense periureteral adhesions makes it undesirable to defer too long, however. The extraperitoneal method is usually chosen, through the incision described under methods of examination.

Ransohoff (Keen's "Surgery," vol. vi) suggests a method apparently far simpler than any in general use. After division of the ureter near the kidney, a blunt uterine curette is slipped over the end and gradually pushed downward toward the bladder; it separates easily from its bed in this way and when the loop of the curette is advanced as far as possible it is pressed up against the skin, which is buttonholed over it, and the enucleated part of ureter is delivered and removed. The method is not applicable when the ureter is greatly thickened and dilated from obstruction by a large stone, cicatrices, or tuberculosis.

URETEROURETERAL ANASTOMOSIS.—This operation is employed to restore the continuity of the duct after accidental division or division during abdominal or pelvic operations; after resection for stricture, ulceration, or sloughing induced by any condition, particularly calculus, and after rupture or other injuries due to external violence.

Four methods have been successfully used: direct end-to-end anastomosis; Poggi's end-to-end invagination of the upper into the lower portion of the ureter; oblique end-to-end anastomosis, as practised by Bovée, and lateral implantation, as suggested by Van Hook. Van Hook's method

is most readily and rapidly performed and is generally preferred. Bovée's method might be employed in case there was great loss of substance. In case more than a third of the circumference of the duct is involved by an injury, division and anastomosis would be the preferable method of treatment.

By *Van Hook's method* the lower end of the ureter is ligated and a longitudinal incision twice as long as the diameter of the ureter is made in its wall $\frac{1}{4}$ inch (6 mm.) below the ligature. The upper end is slit up $\frac{1}{4}$ inch (6 mm.) and 2 very small sewing needles threaded on one fine suture of sterilized catgut are passed through its wall from within outward, $\frac{1}{8}$ inch (3 mm.) from its extremity, and $\frac{1}{16}$ inch (1.5 mm.) apart. These needles are carried through the slit in the lower end of the ureter into and down the tube for $\frac{1}{2}$ inch (13 mm.), and are then pushed through its wall side by side. By traction on the catgut loop the upper end of the duct is drawn into the lower portion and the ends of the loop are tied. Although catgut was originally used because its early absorption lessened the danger of the formation of calculus, silk is to be regarded as a safer suture material and no bad results have been reported from its use.

The site of the union is then enveloped in peritoneum, which is stitched in place about it.

The following method of approaching the lower part of the ureter has been employed by the writer in 6 cases. The first patient operated on was a boy 18 years of age with diverticulum of the bladder. A median suprapubic incision was made from the symphysis to the umbilicus, extending through the fascia between the recti

muscles down to the peritoneum. The peritoneum was brushed back from the fundus of the bladder and the latter lifted forward and opened to explore and pack the diverticulum. Dissection was carried down to the base of the bladder, exposing and freeing the ureter for 2 or 3 inches. The diverticulum having been removed, the opening in the bladder was closed, complete recovery following.

In the second and third cases the operation was performed for stones in the lower ureter. The ureter was exposed as in the preceding case, except that the bladder was not opened. The other 3 cases consisted of extra-peritoneal resections of the bladder for cancer. Judd (*Annals of Surg.*, Mar., 1914).

In the dog ureteroureteral anastomosis is a satisfactory procedure. If a gap of 1 to 2 cm. is left between the several ends, tubulization will take place around the catheter (the latter having been covered by peritoneum sutured loosely around it). In clinical cases of ureteral injury, ureteroureteral anastomosis should be preferred because it attempts to restore the physiologic condition. If stenosis follows such an operation, the ureter can easily be dilated from time to time, since cystoscopy has been so simplified that catheters or bougies are readily inserted into the ureters. While healing occurs, with the catheter still *in situ*, the catheter can be manipulated whenever necessary until a tract is formed bridging a gap between the severed ureteral ends. M. Joannides and C. K. Holmes (*Jour.-Lancet*, Oct. 1, 1925).

URETERAL IMPLANTATION

into the bladder, into some portion of the intestine, and onto the skin has been suggested by many operators and by numerous methods. Such operations are undertaken for the cure of ureteral fistulæ, the prevention of fistulæ in case too great injury has been done to the ureter to permit of anastomosis, in cases of exstrophy of

the bladder, and for ureterouterine and ureterovaginal fistulæ.

In cases of ureterovaginal fistulæ Kelly recommends making a vesicovaginal fistula near by, then inclosing both fistulæ in a circular denudation and suturing the sides together.

Ureterocystotomy.—In this procedure the abdomen is opened and the end of the ureter is freed. An incision is made at a suitable place in the bladder wall; long forceps are introduced into the bladder through the urethra and are used to pull the ureter through the bladder incision, into which it is sutured by fine silk interrupted sutures.

Implantation into the bowel has been performed many times, but infective nephritis has frequently resulted. The sigmoid flexure, or the ascending or descending colon, has been most often selected. Fowler described a method by which he operated successfully on a boy 6 years old for exstrophy of the bladder. After opening the abdomen and isolating the ureters, a longitudinal incision 7 cm. long was made on the anterior wall of the rectum through the serous and muscular coats; the coats were dissected back until a diamond-shaped space on the submucous coat was exposed. A tongue-shaped flap with its base upward was cut in the mucous membrane of the lower half of the diamond. The flap was doubled up, approximating the submucous surfaces, and secured with sutures; thus, a flap-valve was secured, both sides of which were covered with mucous membrane. The ureters were then placed in the incision with obliquely cut ends presenting on the external surface of the flap, and were secured by a few

stitches in the upper half of the diamond; the flap with the attached ends of the ureters was then pushed into the rectum. The gap in the mucous membrane was closed by catgut sutures and then the original wound in the rectal wall was closed by fine silk sutures. The valve-flap and compression of the circular muscular fibers of the rectum combine to prevent the passage of feces into the ureter during defecation.

C. H. Mayo's procedure in ureteral transplantation for bladder exstrophy described thus: The right ureter is first divided about 2.5 cm. from the bladder wall. A longitudinal incision is made through the rectosigmoid opposite the ureter down to the mucosa; the latter is merely punctured. The ureter, slit up for 0.6 cm., is drawn into the bowel by a suture fixed to its end, the needle emerging 1.2 cm. below it, in which position it is anchored by tying the suture externally on the bowel. Interrupted sutures approximate the intestinal muscle over it, alternate sutures catching a bit of the outer wall to hold it securely. Another continuous row of sutures is added. The ureter, thus covered internally for 3 cm. by the mucosa, is closed by any internal pressure, but is opened by outflowing urine. The left ureter is transplanted 10 to 14 days after the right, and the mucosa of the bladder excised by knife or cautery later. The operative mortality was 3.5 per cent. (1 out of 28 cases in which both ureters were transplanted). There were 4 deaths, however, following transplantation of the 1st ureter. In all the cases later traced the functional results were good, though several had died from causes unconnected with the operation. C. H. Mayo and W. Walters (Jour. Amer. Med. Assoc., Feb. 23, 1924).

INJURIES OF THE URETER.

—Aside from the wounds which occasionally occur during surgical operations, injuries of the ureter are ex-

ceptionally rare. Three classes of injuries have been reported: Subcutaneous injuries by indirect violence through the unbroken abdominal wall; injuries from penetrating wounds, and wounds inflicted during operations.

Symptoms.—In some cases there is hematuria, which is usually slight and transient. If the rupture has not also torn into the peritoneal cavity, a tumor forms, due to the escape of urine into the areolar tissue. The fluid aspirated from such tumors has the characteristics, more or less pronounced, of urine. As soon as the urine and blood begin to decompose, inflammation and suppuration, with their attendant symptoms, occur. When the injury communicates with the peritoneal cavity, symptoms of peritonitis, which is usually fatal, occur.

Treatment.—The ideal treatment is immediate suture or anastomosis, but unfortunately the exact injury is not usually recognized until some time has elapsed and the peritoneum has become infected or a retroperitoneal cyst has formed. In case a cyst has formed, **puncture** may be tried, but the result is uncertain. **Lumbar incision, with evacuation of the extravasated fluid and drainage,** offer the most favorable conditions for repair. Wounds of the ureter usually heal ultimately without suture, although, if the injury be found, it should be repaired. **Nephrectomy** will be required if there is evidence of extensive suppuration, septic nephritis, or a permanent fistula that is a source of intolerable discomfort.

W. W. KEEN,
Philadelphia,
AND
M. B. TINKER,
Ithaca, N. Y.

KINÓ.—Kino (resin kino; gum kino) is the inspissated juice of *Pterocarpus marsupium*, a leguminous tree of the East Indies, including southern India and Ceylon. It is obtained from incisions into the trunk, the juice exuding from which is allowed to dry in the sun. It occurs in fragments of a dark-red color (in thin layers ruby-red), without odor, and of a sweetish, strongly astringent taste. It is soluble in alkalies, and usually dissolves to the extent of 80 per cent. in boiling water and in cold alcohol, but is only partially soluble in cold water, and almost insoluble in ether. Its most important constituent is *kinotannic acid* ($C_{18}H_{16}O_8$), of which it contains 40 to 80 per cent. It also includes *kinoin*, a crystalline neutral substance yielding *kino red* on hydrolysis; *gallic acid*, *pyrocatechin*, *pectin*, resin, gum, etc. Upon exposure of a solution of kino to the air, the insoluble, amorphous substance, *kino red*, is deposited.

PREPARATIONS AND DOSE.—*Kino*, U. S. P. (kino). Dose, 5 to 30 grains (0.3 to 2 Gm.); average, 8 grains (0.5 Gm.).

Tinctura kino, U. S. P. (tincture of kino), made from 10 parts of kino, upon which are poured 50 parts of boiling water; this mixture is heated for 1 hour on a water bath, with frequent shaking, then cooled, and 500 parts of alcohol added. To be kept in small, well-stoppered bottles. Dose, $\frac{1}{2}$ to 2 fluidrams (2 to 8 c.c.).

Tinctura kino et opii composita, N. F. IV (compound tincture of kino and opium), every fluidram (4 c.c.) of which represents $\frac{1}{2}$ grain (0.03 Gm.) each of kino and opium. Dose, 1 fluidram (4 c.c.).

Pulvis kino et opii compositus, N. F. IV (compound kino powder), consisting of a mixture of 15 parts of powdered kino with 4 of cinnamon and 1 of powdered opium. Dose, 15 grains (1 Gm.).

PHYSIOLOGICAL ACTION.—The physiological action of kino may be said to be that of its main constituents, kinotannic and gallic acids, especially the former. It is an astringent and styptic, exerting its activity in these particulars throughout the length of the intestinal tract. Its value in arresting intestinal hemorrhage is thus explained.

THERAPEUTICS.—Kino is a mild astringent. It is useful in *serous diarrhea*,

for which purpose it is generally combined with paregoric and chalk mixture, or exhibited in the form of the compound powder of kino, of which 5 to 20 grains (0.3 to 1.25 Gm.) are given at a dose. Kino is a serviceable remedy in *pyrosis*.

Locally and internally kino possesses some value as an hemostatic in passive *hemorrhage from the intestines* and other viscera. The tincture may be used as an astringent gargle in *pharyngitis* or for *relaxation of the uvula*. It is a not infrequent ingredient of injections in *gonorrhea* and *leucorrhea*. The powder may be applied as a stimulating astringent dressing to *chronic ulcers*. In relaxed conditions of the mouth and throat and in *epistaxis* the tincture may be used with benefit. S.

KNOCK-KNEE. See ORTHOPEDIC SURGERY.

KOLA (Soudan coffee; Bichy nuts; cola; Guru or Gooroo nuts) consists of the recent or dried cotyledons of *Cola vera* Schum, or of *Cola acuminata* (Schott), from tropical Africa and the West Indies. When fresh the nuts are either white or purplish red. The natives use the fresh kernels, usually after these have been caused to germinate, because they are then sweeter. The color changes on keeping to a dull purplish brown. When thoroughly dried these nuts keep well indefinitely. Kola seeds contain fat, 0.1 per cent. of volatile oil, from a trace to 4 per cent. of sugar, more than 40 per cent. of starch, 1.7 to 4 per cent. of kola tannin, and 1.5 to 3.6 per cent. of total alkaloids, of which $\frac{1}{100}$ to $\frac{1}{40}$ is theobromine ($C_7H_8N_4O_2$) and the rest is caffeine ($C_8H_{10}N_4O_2$). The caffeine percentage in kola increases on drying.

PREPARATION AND DOSE.—The drug is semi-official:—

Kola, N. F. (kola; cola), containing at least 1 per cent. of caffeine. Dose, 60 grains (4 Gm.).

Fluidextractum kola, N. F. (fluidextract of kola); 100 c.c. to yield 0.85 to 1.15 Gm. of caffeine. Dose, 1 fluidram (4 c.c.).

THERAPEUTICS.—Kola is employed for the same purposes as caffeine. It has been recommended for the treatment of *cardiac failure*, *tropical diarrhea*, *head-*

ache, neuralgia, migraine, and in nervous breakdown from overwork. It has been claimed that the nut when eaten increases the power to endure fatigue without food. In **asthenia** the drug sometimes affords immediate and permanent relief, especially if the condition is of nervous origin. Kola is a decided diuretic, more prompt and efficacious than digitalis and caffeine in combination (Tarbrough). It affects the kidney directly and, in addition, raises the blood-pressure. Kola is further used in **melancholia**, in **chronic alcoholism**, and in **morphinism** as a stimulant and against the shock of the withdrawal of the accustomed drug. It is of service also in **insomnia** from fatigue and exhaustion.

W.

KOUMISS AND KEFIR.—Koumiss (kumiss; kumyss; lac fermentatum) consists of milk which has been altered by both lactic acid and alcoholic fermentation, the latter process taking place through the agency of yeast. Kefir (kephir; kapor; kephir-kumyss) is milk—originally mare's milk—subjected to fermentation by *Streptococcus kefir*, an organized ferment occurring in large granules; as in the case of koumiss, lactic acid fermentation takes place simultaneously. In this country kefir is usually made with the so-called "kefilac" tablets.

PREPARATION.—Koumiss: Fresh cows' milk, 1000 c.c.; compressed yeast, 3 c.c.; sugar, 35 Gm. Dissolve the sugar in the milk, contained in a strong bottle; add the yeast, cork the bottle securely, and keep it at a temperature between 73.4° and 89.6° F. (23° and 32° C.) for six hours; then transfer to a cold place (National Formulary).

A formula by G. Carroll Smith for home-made koumiss is the following: Boil fresh milk, and when nearly cold put into quart bottles, leaving room enough to shake. Add ½ ounce of granulated sugar and a piece of Vienna yeast the size of a hazelnut; cork with new corks, tie down, keep cool, lay the bottles horizontally, but shake twice daily. The preparation is ready for drinking on the sixth day, or earlier in hot, later in cold, weather. The koumiss can be made thinner by using skimmed milk.

Instead of preparing koumiss with

sweet milk, and waiting for it to turn sour, 1 part of ready-made koumiss may be added to 2 parts of fresh milk, the casein being thus precipitated at once. Although in this case yeast is not necessary, sugar must be added to produce sufficient carbonic acid gas to make it effervescent.

Koumiss may be made from sour milk, freed from its cream, by breaking up the curd by strong stirring, and adding the sugar and yeast.

Kefir may be prepared by adding active kefir grains or 1 kefilac tablet to 1 pint (½ liter) of fresh cows' milk and keeping it at a temperature of 70° to 80° F., until the grains rise to the surface or, in case the kefilac tablet has been used, forty-eight hours.

The grains may then be strained off for further use. The milk will retain sufficient yeast-cells to cause it to ferment if put aside in well-stoppered bottles. The bottle should be shaken 4 or 5 times a day until ready for use, and thereafter whenever part of the contents is to be poured off.

THERAPEUTICS.—Koumiss and kefir provide most of the elements of milk in an agreeable, readily digestible form, and are of distinct value in cases where milk is not well borne or for some other reason cannot be taken. They differ in composition from cows' milk in containing only about 1.5 per cent. of milk-sugar, and in including 2 per cent. of alcohol and nearly 1 per cent. of lactic acid. The casein is present in so finely divided a state that it cannot form lumps in the stomach and is thus readily digested by the gastric juice.

Both koumiss and kefir, when ingested, tend to increase the appetite, cause an agreeable sensation of warmth in the stomach, and augment the desire for fluid intake. Constipation is overcome, and either the renal or the sweat function is increased, according to the prevailing air temperature. Deposition of fat in the organism is favored. Slight drowsiness may be noted. Where diarrhea is produced, lime water may be added to either preparation.

Therapeutic use of koumiss and kefir was first made in **pulmonary tuberculosis**. In the Russian koumiss cure the koumiss

is given at short intervals during the day—but not for two hours previous to heavy meals—and in ascending amounts.

In quantities of from 1 pint to 2 quarts ($\frac{1}{2}$ to 2 liters) they have been of good service in gastric disorders, such as **cardialgia**, **catarrh**, **atony**, **dilatation**, **vomiting**, **digestive disturbances**, and **gastric ulcer**. In **hypochlorhydria** the use of kefir increases the hydrochloric acid. Cases of severe **diarrhea** are benefited by kefir. Its main indication is in **autointoxication** due to the intestinal putrefaction of protein substances. Kefir is contraindicated in hyperpepsia with retarded emptying of the stomach and with excessive secretion, as well as in pyloric stenosis. In general, it should not be used in gastric ulcer, though in chronic cases with slight secretion it may be of great value.

A point of special interest is the possibility of adding various drugs to kefir during or after its preparation, *e.g.*, lactate of iron, arsenic, iodides, creosote, and guaiacol. Substances which do not inhibit fermentation may be added when the ingredients of the kefir are first mixed; creosote and guaiacol are best added to the finished product. W. and S.

KOUSSO. See **CUSO**.

KRAMERIA.—*Krameria* (rhatany), named after J. G. H. Kramer, a Hungarian physician and botanist (Tschirsch), is the dried root of *Krameria triandra* (Peruvian krameria) or of *K. argentea* (Para or Brazilian krameria), small shrubs of the family Leguminosæ.

The Peruvian variety of rhatany or krameria is also obtained from Bolivia, and the Savanilla krameria from Colombia, British Guiana, and Brazil. The bark of the root is strongly astringent in taste, but almost devoid of odor. The woody part is inodorous and tasteless, and is relatively inactive. The smaller roots are therefore preferred. *Krameria* contains 8 to 20 per cent. of **kramerotannic acid** (the active ingredient), gum, starch, sugar, and a peculiar acid called **krameric acid**. *Krameria*, in common with kino, is an ingredient of the **pulvis catechu compositus** (B. P.).

PREPARATIONS AND DOSE.—*Krameria*, U. S. P. (*krameria*; *rhatany*). Dose,

5 to 30 grains (0.3 to 2 Gm.); average, 15 grains (1 Gm.).

Tinctura krameria, U. S. P. (tincture of krameria), a 20 per cent. preparation. Dose, $\frac{1}{2}$ to 2 fluidrams (2 to 8 c.c.).

Extractum krameria, N. F. (extract of krameria). Dose, 5 to 20 grains (0.3 to 1.25 Gm.); average, 8 grains (0.5 Gm.).

Fluidextractum krameria, N. F. (fluid-extract of krameria). Dose, 5 to 30 minims (0.3 to 2 c.c.); average, 15 minims (1 c.c.).

Syrupus krameria, N. F. (syrup of krameria), made by mixing 9 parts of fluid-extract of krameria with 11 parts of syrup. Dose, 20 to 90 minims (1.25 to 6 c.c.); average, 1 fluidram (4 c.c.).

Trochisci krameria, U. S. P. VIII (troches or lozenges of krameria), made by mixing together 6 parts of powdered extract of krameria, 65 parts of sugar, and 2 parts of tragacanth, forming a mass with stronger orange-flower water, and dividing into troches. Each lozenge contains 1 grain (0.06 Gm.) of extract of krameria.

Tincture of *Savanilla rhatany* (*K. ixina*, not official) forms a clear solution, tincture of Peruvian rhatany a cloudy mixture, with water (Kraemer).

PHYSIOLOGICAL ACTION.—The kramerotannic acid imparts to krameria its astringent properties. The drug seems to act particularly well upon the mucous membranes, and its beneficial influence in all conditions characterized by relaxation of the latter is pronounced. It is better borne when taken internally than tannic acid.

THERAPEUTICS.—*Krameria* is used largely as a remedy for bowel disorders, *viz.*, in **chronic diarrhea**, in **dysentery**, and in passive **hemorrhage from the intestines** and other viscera. A 5 to 10 per cent. aqueous solution of the fluidextract for daily irrigation of the lower bowel in **colitis** is useful. Swan recommends the following in chronic diarrhea:—

℞ *Acidi sulphurici aro-*

matici fʒss (15 c.c.).

Tr. opii camphorata .. fʒj (30 c.c.).

Extracti hamatoxyli .. ʒss (15 Gm.).

Syrupi krameria fʒiiss (45 c.c.).

Aqua cinnamomi q.s. ad fʒvj (200 c.c.).

M. Sig.: Two teaspoonfuls in water every three hours.

In **leucorrhea** and **gonorrhea** the astringent action of **krameria** may be availed of. **Chronic pharyngitis** and inflammatory conditions of the respiratory mucosæ are generally benefited, though tannic acid is more convenient to use and effective. **Spongy gums** and **anal fissure** are among the numerous local conditions in which

krameria has proven useful. The drug may be employed in a 10 per cent. ointment or, in **hemorrhoids**, in a suppository containing 15 grains (1 Gm.) of **krameria**, with or without cocaine, epinephrin, etc.

S.

KRAUROSIS VULVAE. See VAGINA AND VULVA, DISEASES OF.

L

LACHRYMAL APPARATUS, DISEASES OF.

SECRETORY APPARATUS, DISEASES OF THE.

DACRYOADENITIS.

Inflammation of the lachrymal gland is of rare occurrence, either in the acute or chronic form. It is indicated by swelling and edema of the upper lid, and pain and tenderness on pressure of the gland and the adjacent supraorbital margin. The disease may assume a purulent form, when an abscess may open, either upon the conjunctiva or through the skin.

Rheumatism, cold, syphilis, septicemia, and mumps have all been ascribed as the cause in various cases, while the spread of inflammation from the conjunctiva and cornea has been noted in a number of instances.

Treatment.—**Hot applications** and **poultices** in the early stages, followed by free **incision** under the supra-orbital region as soon as pus has formed. In the chronic variety the local application of absorptive ointments, such as the **mercurial** and the **compound iodine ointments**, should be employed, while **potassium iodide**, **mercury**, and the **salicylates** should be administered internally. In acute cases an active **calomel purge** should be prescribed, followed by large doses of **quinine**.

TUMORS, such as sarcoma and adenoma, and hypertrophy of the gland are of rare occurrence. The latter is at times of congenital origin, but is usually an affection of later years. The gland may attain a large size, and cause serious damage to the eyeball by compression.

Treatment.—**Extirpation** of the gland is indicated in cases of neoplasms and extreme hypertrophy, or where there is obstinate stillicidium which cannot be controlled in any other way. This is accomplished by removing the gland, either directly through a skin incision made over the gland, or by an incision through the conjunctiva after exposure of the *cul-de-sac*, by division of the external canthus. The latter procedure is the one usually employed, as the ptosis which is apt to follow the first mentioned, due to injury of the levator, is avoided, and the resultant scar is much less conspicuous.

ATROPHY of the lachrymal gland is very rare, being usually associated with xeroma of the conjunctiva.

DACRYOPS is the name given to a cystic disturbance of one of the ducts of the gland, and occurs as a bluish-pink, translucent, elastic tissue, which is found under the conjunctiva in the region occupied by the gland.

LACHRYMAL FISTULA may form occasionally as a sequel of inflammation or traumatism of the gland, and may cause a constant discharge of tears through its orifice. A similar condition has also been observed of congenital origin.

DISLOCATION OF THE LACHRYMAL GLAND has been met with in a few instances as a result of trauma, and in a very few in which the prolapse was congenital. In other rare instances it was spontaneous in origin.

EXCRETORY APPARATUS, DISEASES OF THE.

In contradistinction to diseases of the secretory portion of the lachrymal apparatus, diseases of the excretory portion are of very frequent occurrence and are all characterized by the common and annoying symptom of tears flowing over the cheek.

ANOMALIES OF THE PUNCTA LACHRYMALIA AND OF THE CANALICULI.

Congenital.—Complete obliteration or absence of the puncta as well as double puncta has been occasionally observed. At times the puncta and canaliculi may be wanting, the canals being represented by narrow grooves along the edges of the lid.

Acquired.—Such anomalies are usually the result of chronic inflammations of the lids and conjunctiva which have disturbed the normal relationship existing between the puncta and the bulbar conjunctiva. They are frequently induced by old age, due to a senile relaxation in the orbicularis palpebrarum, and are constantly present in paralysis of the seventh nerve.

Eversion of the punctum is almost

a constant consequence of ectropion, and is also present in those rare cases when the eyeball is so deeply set that a triangular space intervenes between the lid and the globe.

Complete obliteration is a not infrequent result of burns and traumatisms which have involved the lids, and of granular conjunctivitis and blepharitis. Rarely, the canal may be blocked by a cilium or polypus, or by leptothrinx.

Symptoms.—The most common symptom of all these anomalies is the constant overflow of tears. This is annoying in itself, but, more than that, it frequently causes such irritation of the skin about the lids that an inflammation is set up which causes contraction of the parts, and still further interference with the proper canalization of the tears.

Hyperemia and catarrh of the conjunctiva are constantly present, consecutive to all forms of lachrymal obstructions.

Treatment.—Usually the simple dilatation of the punctum, or the slitting up of the canaliculus, is sufficient to effect a cure, with the co-operation of an astringent wash of zinc and boric acid.

If the condition has been brought about, however, by a high degree of ectropion, or is the result of an extensive burn, relief will be frequently difficult to attain, and extensive plastic operations may be necessitated before the lid is restored to its normal position.

ANOMALIES OF THE LACHRYMAL SAC AND NASAL DUCT.

DACRYOCYSTITIS, or inflammation of the lachrymal sac, may be either acute or chronic.

Symptoms.—The disease is rarely acute, but begins generally as a chronic inflammation, which manifests itself by a slight swelling and redness at the inner canthus, and by persistent and troublesome lachrymation, or by the discharge of a mucopurulent secretion from the inner canthus of the eye. Pressure on the sac will express a secretion which is either mucoid or mucopurulent, either into the conjunctival *cul-de-sac* or into the nose. This condition of affairs may persist and the sac may become chronically disturbed, and give rise to a tumor of considerable size (lachrymal tumor, or mucocele). Frequently the inflammation assumes an acute form, and the region of the sac becomes swelled and reddened and a thick, creamy pus forms in the sac, which is only expressed after some difficulty. The pain is intense, and there are marked constitutional symptoms, such as fever and loss of appetite. If the parts are undisturbed, the skin ulcerates and is perforated, usually beneath the tendon of the orbicularis muscle, and a permanent fistula is formed. More rarely, the opening in the sac heals, and the formation of the fistula is avoided. As a result of the fistulous formation, pus frequently burrows into the deeper tissue, and necrosis of the neighboring bones is not rarely occasioned.

Etiology.—In the great majority of cases dacryocystitis is secondary to diseases of the lachrymonasal duct, primary inflammation of the lachrymal sac being an extremely rare affection. It is a disease of adults, being rare in children, when it occurs under 10 years of age being usually significant of inherited syphilis.

Treatment.—As inflammation of the lachrymal sac is dependent in most cases upon disease of the lachrymal duct, any obstruction existing there should be combated in the manner presently to be described. If this has been neglected, however, and an acute exacerbation has been inaugurated, **hot applications** should be made to the tumor, and any **pus evacuated** by **incision** into the sac through the dilated lower canaliculus as soon as its presence is manifested. A lead style should then be inserted into the duct and allowed to remain *in situ* for several months until the patulency of the canal is restored. **Calomel** and **quinine** should be administered internally.

STRICTURE OF THE LACHRYMAL DUCT.

SYMPTOMS.—These are the same as in the first stages of dacryocystitis, and consist chiefly in obstinate lachrymation and in the ability to express a viscid matter into the *cul-de-sac* by pressure with the finger upon the lachrymal sac.

Stricture of the lachrymal duct is favored greatly by its relationships and by the anatomy of its parts. The mucous membrane which lines the bony walls of the canal is very vascular, and at certain parts is thrown into folds, which swell under slight provocation and offer sufficient obstacle in themselves to prevent the proper canalization of the tears. Again, the duct bears such a close relationship to the nose that it is necessarily exposed to all inflammations of this cavity. Indeed, the great majority of cases of lachrymal obstruction are secondary to acute or chronic disease of the nose. This is

particularly true of nasal disease of syphilitic origin. As a consequence of its liability to inflammation by direct continuity of structure, the nasal end of the duct is the most frequent seat of stricture, the commencement of the duct at the extremity of the lachrymal sac offering the next most favorable site for the development of stricture.

TREATMENT.—While an absolute and a complete cure of lachrymal obstruction may be frequently attained, more often relief is only partial.

Treatment may be either palliative or curative. The former consists in repeatedly **pressing the contents of the lachrymal sac into the nose** by the finger, and by the employment of **antiseptic and astringent eye-washes**, or by throwing a stream of **boric acid solution** into the sac by means of an Anel syringe. Attention must be directed toward the nasal mucous membrane, and any local irritation existing about the nasal opening of the duct must be controlled with local applications.

The curative plan of treatment resolves itself into some form of **surgical procedure**. These measures have been conveniently classed by Theobald under four heads: 1. Those which aim to restore the natural passages. 2. Those which have for their object the formation of a new passage into the nose for the tears. 3. Those which aim at the obliteration of the natural passages,—the lachrymal sac and duct. 4. The removal of the lachrymal gland for the purpose of arresting the secretion of tears.

The first step toward the restoration of the natural passages consists in the **operation of Bowman**, which

consists in **slitting up the lower canaliculus throughout its entire length**. This is accomplished by entering a fine canaliculus knife into the inferior punctum, and by slowly pushing it along the floor of the canaliculus until it abuts against the inner wall of the sac, as it rests against the lachrymal bone. The handle of the knife should now be swept upward, while an upward and slightly backward inclination is given to the blade of the knife.

A ready and free entrance into the sac being gained by the successful accomplishment of this act, attempts should be made to engage the stricture, and to **dilate** its caliber by means of **probes**. I generally first make the attempt with a very small Bowman probe, and then gradually increase the size by passing slightly higher numbers every second or third day. I am satisfied after a No. 8 probe can be passed into the nose without difficulty. Larger probes are not employed, as they are apt to injure the mucous membrane and periosteum, and in some cases to lead to necrosis. Weber, Cooper, and Theobald, however, think sounds of the size of a Bowman No. 8 quite inadequate, and have devised probes of much larger caliber, employing instruments of a diameter of 4 mm. in the treatment of the majority of their cases. As stated above, I am generally satisfied with a moderate dilatation, and alternate the passage of probes with careful **syringing of the duct with a weak solution of zinc and boric acid**.

In infants operative procedure should be postponed until palliative measures have been thoroughly tried, although in obstinate cases this may

be successfully accomplished under a general anesthetic.

To prevent closure of the duct after it has been made patulous, a number of operators insert a **leadén style**, leaving this in position for several weeks or months. This is of especial value when the patients live at a distance, and cannot submit to the frequent and continued probing which is necessary to attain the best results.

Other surgeons prefer **rapid dilatation**, and insert probes of the largest size into the duct at the first sitting, this being usually performed under ether.

Should the lachrymation still persist after probing has been given a thorough trial, I resort to leadén styles, permitting them to remain *in situ* for months and even years. Care should be taken that the head of the style rests securely in the groove of the slit-up lower canaliculus to insure the patulency of that structure. The insertion of the style into the duct is greatly facilitated by the use of the **Ziegler style inserter**.

In intractable cases—as, for example, when the stricture is bony—two procedures have been practised: the **removal of the lachrymal gland** and the **obliteration of the lachrymal sac**. The former of these has been modified by de Wecker, who excises the little lobules and the emissary ducts from both the subsidiary and main lachrymal glands.

Extirpation of the sac should be resorted to in all cases of long-standing lachrymal disease where the mucous membrane has become chronically inflamed and continued local astringent treatment, with probing, has been unavailing. The procedure also is indicated in lachrymal mucocele, in

fistulæ, and in all suppurative conditions. If performed with extreme care after the method described by Meller, of Vienna, scarring is slight and the resultant epiphora of but little annoyance.

Toti has recommended an **operation** which aims to relieve the symptoms produced by stricture of the lachrymal duct by establishing a connection between the sac and the roof of the nose, by means of a resection of the lachrymal bone and excision of a portion of the external wall of the sac. A number of modifications of Toti's original technique have also been described by various operators.

WILLIAM CAMPBELL POSEY,
Philadelphia.

LACTATIONAL INSANITY.

See PSYCHOSES.

LACTIC ACID.—The official lactic acid (*acidum lacticum*, U. S. P.) is a colorless, nearly odorless, syrupy liquid having a very sour taste and a specific gravity of 1.206 at 25° C. It is hygroscopic, and is miscible in all proportions with water, alcohol, and ether, but is insoluble in chloroform, carbon disulphide, and petroleum benzin.

PREPARATION AND DOSE.—*Acidum lacticum*, U. S. P. (lactic acid), contains 85 to 90 per cent. of absolute lactic acid. Dose, 15 to 30 minims (1 to 2 c.c.).

PHYSIOLOGICAL ACTION.—Lactic acid is present in the stomach during the digestion of carbohydrates, especially during the first stage of gastric digestion, when, in excess, it forms one variety of sour stomach and causes pain in different parts of the body, headache, etc. Rheumatoid symptoms sometimes develop after the drinking of sour milk. Large amounts depress the nervous system and decrease the alkalinity of the blood.

THERAPEUTICS.—Lactic acid is a caustic, astringent, digestive, and antidiabetic remedy. It has been used, diluted, in **dyspepsia**, **diarrhea**, **croup**, **cholera**; in pure form, as a solvent of false mem-

branes; in tuberculous affections of the mouth, esophagus, and larynx; in lupus, and in alopecia.

LACTUCARIUM.—*Lactucarium* ("lettuce opium") is the concrete milk-juice of *Lactuca virosa*, family Compositæ, a wild variety of lettuce growing in Europe. It occurs in irregular, brown lumps, wax-like internally, with an opium-like odor. It is partly soluble in alcohol, and about 50 per cent. of it will dissolve in water. It contains, among other substances, *lactucin*, a bitter principle. Hyoscyamine is said to have been found in it. It is no longer official.

PREPARATIONS AND DOSE.—*Lactucarium*, U. S. P. IX (*lactucarium*). Dose, 15 grains (1 Gm.).

Syrupus lactucarii, U. S. P. IX (*syrup of lactucarium*), contains 10 per cent. of the tincture. Dose, 1 fluidram (4 c.c.).

Tinctura lactucarii, U. S. P. IX (*tincture of lactucarium*), 50 per cent. Dose, 10 to 60 minims (0.6 to 4 c.c.).

PHYSIOLOGICAL ACTION.—*Lactucarium* has been credited with hypnotic properties, but more recent experience has shown that this action is very feeble or *nil*. Half an ounce has been given to a dog without result.

THERAPEUTICS.—*Lactucarium* has been chiefly used in slight irritation of the larynx and to allay nervous irritability. The syrup may be used in cough mixtures for children and delicate subjects, and also, for general sedative purposes in children, as vehicle for and adjuvant to bromides. *Lactucarium* lozenges for cough are on the market. At least one of the proprietary lozenges has been found to contain opium. *Lactucin* may be tried as an hypnotic and sedative in the dose of 1 to 2 grains (0.06 to 0.12 Gm.).

LARYNGOSCOPY, BRONCHOSCOPY, AND ESOPHAGOSCOPY.

LARYNGOSCOPY, INDIRECT.

This consists of inspection of the interior of the larynx with a mirror held in the fauces of the patient. The mirror serves both for the reflection of light into the larynx and for reflection of the image into the ob-

server's eye. It is called *indirect* because of the inspection by reflected image, in contradistinction to direct laryngoscopy (*q.v.*), in which the interior of the larynx is seen directly.

Indirect, or mirror, laryngoscopy remains the most valuable of all means for laryngeal diagnosis in adults and older children; under four years of age the mirror is useless. Fortunately, the direct method is very satisfactory at any age, even in the newborn. For all operative procedures, however, the anteroposterior reversal of the image by the mirror, as well as other technical difficulties, have led to the general preference for the direct method.

Useful examination of the larynx by any method requires practice under an instructor.

LARYNGOSCOPY, DIRECT.

Direct laryngoscopy refers to the examination of the interior of the larynx by means of a laryngoscope, which is practically a laryngeal speculum. It is called *direct* in contradistinction to indirect laryngoscopy (*q.v.*), in which the mirror image and not the larynx itself is seen.

The form of laryngoscope most commonly in use for both adults and children is shown at *A*, in Fig. 1. With it the larynx of even a newborn baby can be examined with perfect safety. It is held in the left hand, while forceps or other instruments are used with the right. This bi-manual manipulation, in practised hands, resembles the coördinate use of a knife and fork at the table, and for this reason is preferred by facile operators. Various forms of apparatus fixed to the table have been devised to suspend an adult patient's head by a spatula inserted posterior

to and below the base of his tongue, the procedure being called *suspension laryngoscopy*. Other laryngoscopic instruments, for adult patients only, constructed on the principle of prying the pharynx open with a screw, have been devised.

Direct laryngoscopy has a wide range of usefulness in the diagnosis

and treatment of disease. Benign growths are removed with the utmost certainty and precision. The recurrent multiple papillomata of children can be superficially removed as often as recurrence takes place. Ultimately cure will result, with normal larynx and good voice, if no violence has been done to the larynx by radium,

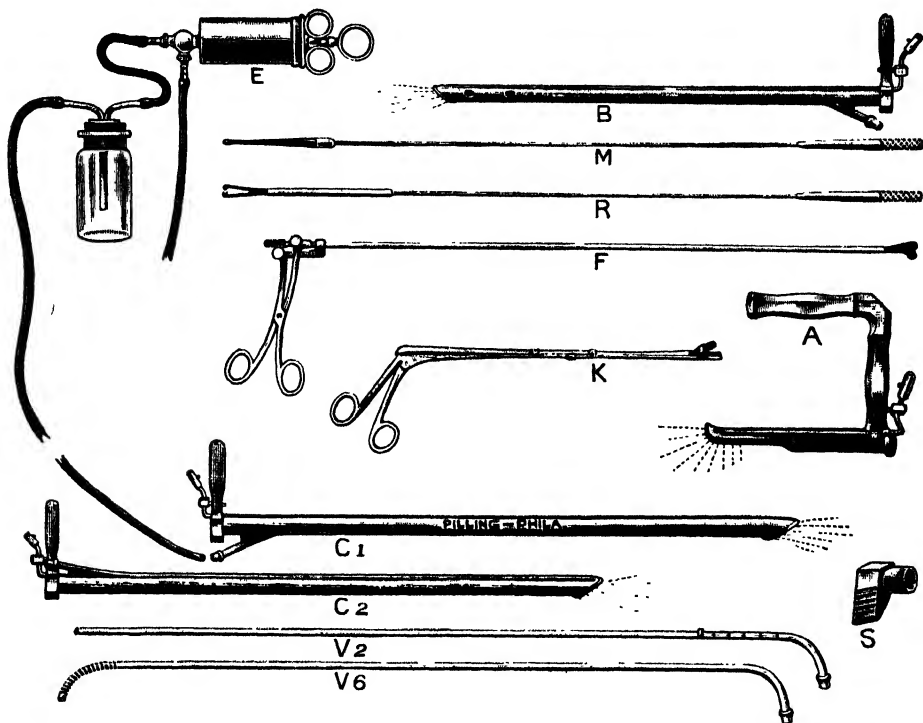


Fig. 1.—Instruments used at the Chevalier Jackson Bronchoscopic Clinic for direct laryngoscopy, bronchoscopy, esophagoscopy, and gastroscopy. Adult's and child's sizes are necessary in tubes and forceps.

B, Bronchoscope: Made with and without an aspirating canal; usually used without a canal, especially in the smaller sizes. **M**, Silk woven, steel-stemmed filiform, for dilatation of strictures under guidance of the eye through the esophagoscope. **R**, Sponge carrier. **F**, Bronchoscopic forceps: Many special forms of jaws are used for special purposes. The side-curved form here shown is most frequently useful. **K**, Laryngeal tissue-forceps for removal of specimens for histologic diagnosis. This form of forceps is made with jaws of different shapes for different purposes, including a generally useful, serrated grasping forceps. **A**, Laryngoscope: This is used for diagnostic and operative work on the larynx and for passing the bronchoscope. It is used also for inspection of the hypopharynx, and may be employed for the introduction of the esophagoscope if desired; but the esophagoscope is generally passed without it. **S**, Moore bite block. **E**, Endoscopic aspirator for use where a portable aspirator is required. It has positive and negative pressure tubes. An electrically driven aspirator is used in the Clinica. **C1**, Standard esophagoscope. The peroral gastroscope is the same except that it is longer. Retrograde gastroscopes and pyloroscopes are shorter. An aspirating canal in the wall of the tube is always used in esophagoscopes and gastroscopes. **C2**, Esophagoscope occasionally used. For most purposes the standard form, **C1**, is better. **V2**, Aspirating tube for removal of secretions. It is used by insertion through the bronchoscope or esophagoscope, as frequently as may be necessary. **V6**, Similar to **V2**, but made with vertebrated tip for reaching "around the corner" in the upper lobe bronchi, or in fistulae anywhere in the lungs.

the Roentgen ray or radical surgery. Specimens of tissue for biopsy can be removed with an accuracy that renders this the final arbiter in the *different*

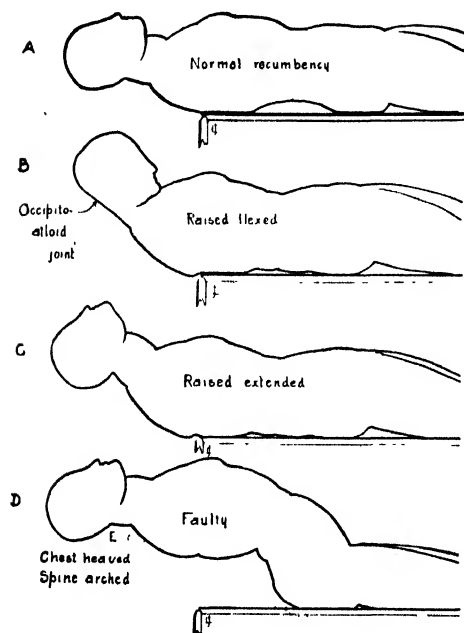


Fig. 2.—Schema of position for endoscopy: **A**, Normal recumbency on the table with pillow supporting the head. The larynx can be directly examined in this position, but a better position is obtainable. **B**, Head is raised to proper position with head flexed. Muscles of front of neck are relaxed and exposure of larynx thus rendered easier; but for most endoscopic work a certain amount of extension is desired. The elevation is the important thing. **C**, The neck being maintained in position **B**, the desired amount of extension of the head is obtained by a movement limited to the occipito-atloid articulation by the assistant's hand placed as shown by the dart (**B**). **D**, Faulty position. Unless prevented, almost all patients will heave up the chest and arch the lumbar spine so as to defeat the object and to render endoscopy difficult by bringing the chest up to the high-held head, thus assuming the same relation of the head to the chest as exists in the Rose position (a faulty one for endoscopy), as will be understood by assuming that the dotted line **E** represents the table. If the pelvis be not held down to the table the patient may even assume the opisthotonos position by supporting his weight on his heels on the table and his head on the assistant's hand; this would render endoscopy exceedingly difficult or impossible. (From a drawing by Chevalier Jackson.)

ential diagnosis between tuberculosis, syphilis, and cancer of the larynx. For this purpose the tissue forceps (similar to **K**, Fig. 1, but having biting basket jaws) are used. The removal of **foreign bodies in the larynx** is accomplished with facility and safety by means of the laryngeal forceps shown at **K**, Fig. 1.

Direct Laryngoscopy for Diagnosis in Children.—It cannot be too strongly emphasized that with the modern technic herein described and the instrument shown at **A**, Fig. 1, there is no longer any need for the usually erroneous, inferential diagnosis as to the cause of *croupy cough* or *laryngeal dyspnea* in children. The larynx can be looked at and swab-specimens from its interior taken in a minute or two, without anesthesia, general or local, in a child of any age, from newborn infancy upward.

Direct Laryngoscopy for the Introduction of Intratracheal Insufflation Tubes.—The introduction of tubes through the larynx is done for various purposes other than bronchoscopy, chief of which are: (*a*) Aspiration of tracheobronchial secretions; (*b*) insufflation of radiopaque substances such as bismuth subcarbonate; (*c*) injection of lipiodol or other radiopaque substances; (*d*) insufflation of vapor of ether for general anesthesia in cases of general surgical procedures about the head or thorax. The laryngoscope (**A**, Fig. 1) is used to expose the upper laryngeal orifice and glottic chink by the technic given below. No anesthetic, general or local, is used in children; local anesthesia is used in adults, except in cases in which ether is to be used by insufflation for a general surgical operation. In the latter class of cases

the insufflation tube is not inserted until after the stage of general surgical anesthesia has been established in the usual way.

Technic of Direct Laryngoscopy.—For *children*, anesthesia, general or

thetia is always dangerous in dyspneic patients. The entire interior of the larynx of any child, even the newborn infant, can be examined in a few minutes without any anesthetic, general or local, and without pain.



Fig. 3.—Position of patient and assistants for introduction of the bronchoscope and esophagoscope: The middle of the scapula rests on the edge of the table; the head and shoulders, free to move, are supported by the assistant, whose arm passes under the neck. The *right* middle finger inserts the bite block into the *left* side of the mouth. The *left* hand, resting on the *left* knee, maintains the desired degree of elevation, extension, and lateral deflection required by the operator. The patient's vertex should be 10 cm. higher than the level (A) of the top of the table. It is essential for the assistant to have constantly in mind that the *right* forearm must not support the neck; all the support must be of the head only and must come from the *left* hand. This is the Boyce position, which has never been improved upon for bronchoscopy and esophagoscopy; but for satisfactory results every detail must be precisely adhered to. (From Chevalier Jackson Bronchoscopic Clinic, University Hospital, Philadelphia.)

local, is quite unnecessary for this procedure; cocaine is dangerously toxic in children, and general anes-

In *adults*, general anesthesia is never required; even local anesthesia may be dispensed with. It is usually

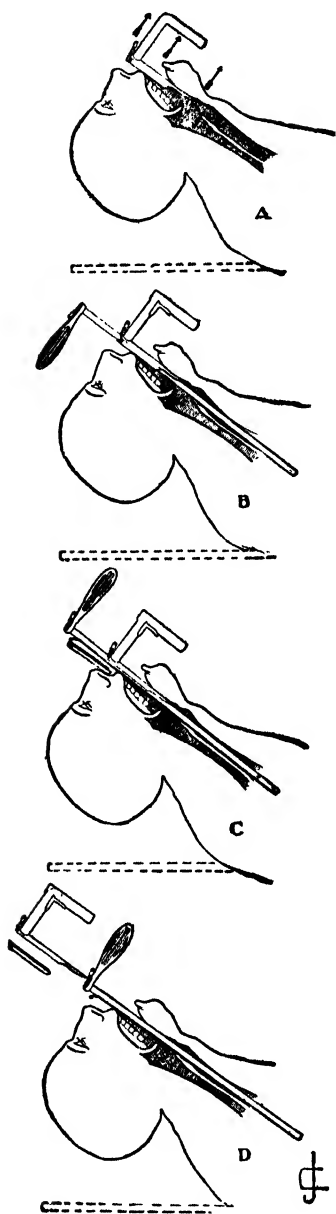


Fig. 4.—Schema illustrating oral bronchoscopy. The portion of the table here shown under the head is, in actual work, dropped all the way down perpendicularly. It appears in these drawings as a dotted line to emphasize the fact that the head must be above the level of the table during the introduction of the bronchoscope into the trachea: *A*, Exposure of larynx. *B*, Bronchoscope introduced. *C*, Slide removed. *D*, Laryngoscope removed, leaving bronchoscope alone in position. ("Bronchoscopy and Esophagoscopy," W. B. Saunders Co.)

advisable, however, in most cases to use local anesthesia in adults, and a sedative may be added if there is no contraindication. **Cocaine** solution in about 8 per cent. strength is applied with a curved laryngeal applicator to the laryngopharynx and pyriform sinuses in the region of the superior laryngeal nerves. This is usually sufficient, but if the laryngeal reflexes still seem too active, a little of the same or a stronger (20 per cent.) solution may be applied to the interior of the larynx with a gauze sponge in the straight applicator (*R*, Fig. 1) after the larynx is exposed to view with the laryngoscope.

The patient is then placed in the position shown in Figs. 2 and 3. The operator must be standing (Fig. 5) and must remain standing during the examination; crouching on the floor will totally defeat the object obtained by the proper position of the patient. The laryngoscope, held in the left hand in the position shown at *A*, Fig. 4, is introduced back along the dorsum of the tongue and the tip of the epiglottis is exposed to view. The lip of the laryngoscope is inserted beyond the proximal edge of the epiglottis for a distance of not more than 1 cm. in a child or 2 cm. in an adult. Then a powerful lifting motion, sufficient to sustain the weight of the patient's head, is imparted to the laryngoscope in the direction of the dart shown at *A*, Fig. 4. At this point particular care to keep the patient's shoulders down on the table is necessary. Prying on the upper teeth as a fulcrum must be avoided. The patient not being anesthetized, there will be no glottic chink until he takes a deep breath. If the patient is three years of age or over he is told to take

a deep breath. If he is under that age he will soon do so without being told.

BRONCHOSCOPY.

Bronchoscopy is a procedure involving the use of an electrically lighted tube (B, Fig. 1) which serves as a speculum. The bronchoscope is introduced through the laryngoscope and the branches of the tracheobron-

It is a highly technical procedure and should not be attempted by the untaught. Further details as to the various conditions in which bronchoscopy is indicated for diagnosis and treatment will be given below.

Contraindications to Bronchoscopy.—There are no absolute contraindications to bronchoscopy for foreign body; there are at times good



Fig. 5.—Proper positions for direct laryngoscopy by the Chevallier Jackson method. Note that the operator is standing. He remains standing throughout the procedure. The nurse has the forceps in presentation position for immediate insertion by the operator; if bronchoscopy were to be done, she would be thus holding the bronchoscope.

chial tree are explored under direct inspection. It is a practical procedure of every-day usefulness in the diagnosis and treatment of diseases of the bronchi and lungs and in the removal of foreign bodies from the tracheobronchial tree and the pulmonary parenchyma. It can be performed, by those who have been properly taught, without any anesthetic, general or local, in children, and without general anesthesia in adults. It is free from mortality in skilled hands.

reasons for postponement. It is well not to repeat bronchoscopy on a child, and especially on a baby, without a few days' interval for recuperation, even though there has been no reaction. At the Chevallier Jackson Clinics we rarely see any reaction after a bronchoscopy, because we make our bronchoscopies brief, and when more than one bronchoscopy is necessary in little children we allow a few days' interval. We have seen no ill-effects from bronchoscopic aspiration of

bronchiectatic cavities once a week for six months; in fact, there is usually a steady gain in weight.

The following list of contraindications to bronchoscopy for disease has been formulated for guidance, but they are all subject to exceptions:—

1. When, in any case of lung-sup-puration not due to foreign body, the pediatrician, the surgeon, and the roentgenologist agree that external surgery is indicated.

pleura can practically always be prevented if the foreign body is removed. If rupture into the pleura has occurred the pleura should be drained externally, but the foreign body, which always remains fixed in the bronchus, should be removed through the mouth.

4. Diffuse suppurative pneumonitis with rapid breaking down of lung-tissue is a contraindication to bronchoscopy when the condition is not due to foreign body. On the contrary,



Fig. 6.—The larynx having been exposed with the laryngoscope, the operator is inserting the bronchoscope through it. The assistant who holds the head has moved out of the way to allow the instruments to be seen.

2. In case of a patient moribund from conditions other than obstruction to the airway.

3. In cases of lung-sup-puration due to causes other than foreign body, and in which rupture into the pleura is imminent. Bronchoscopy is contra-indicated in these cases, not because it would hasten rupture, but because it would be powerless to prevent it, if imminent. In foreign body cases, on the contrary, rupture into the

when such a condition is due to foreign body immediate bronchoscopic removal of the foreign body will promptly stop the whole process, and is the best means for prophylaxis of chronic suppuration. Over and over again bronchoscopists are asked, "Would it not be better to wait until the 'pneumonia' is over before bronchoscopically removing the foreign body?". The answer is emphatically, "No," and it is necessary to add that the

signs of the supposed pneumonia will promptly disappear after the removal of the foreign body.

5. As pointed out by Joseph S. Wall, all manipulations in babies must be gentle.

6. Lack of training, organization and an adequate armamentarium is an absolute contraindication to bronchoscopy in very young children.

Introduction of the Bronchoscope.

—General anesthesia is not necessary

with the direct laryngoscope held in the left hand, as described under DIRECT LARYNGOSCOPY, the insertion of the bronchoscope is easy. Before inserting the bronchoscope a gauze sponge moistened with 20 per cent. solution of cocaine is passed between the cords and down to the bifurcation of the trachea, where it is held for a minute or two. The bronchoscope, illuminated with its own lamp, is passed to the operator in exactly the



Fig. 7.—Chevalier Jackson's method of high-low esophagoscopy; first stage.

and is dangerous in dyspneic patients. **Cocaine** is dangerous and quite unnecessary for bronchoscopy in children; but it is generally used in adults. **Morphine** in full doses may be given to either adults or children and should be administered hypodermically at least 1½ hours beforehand. The patient must be in the position shown in Figs. 2 and 3, and the operator should stand up as shown in Fig. 5 until the distal end of the bronchoscope is in the trachea (*D*, Fig. 4).

Once the vocal cords are exposed

proper position for insertion (point forward, "handle" to the right). The operator, after inserting the bronchoscope in the laryngoscope, transfers his eye to the bronchoscope and, making sure of the presentation of the vocal cords, insinuates the slanted end of the bronchoscope carefully between them.

The exploration of the tracheobronchial tree is a matter of following the lumen, and is greatly facilitated by the position above described (Figs. 2 and 3), which leaves the head of the

patient free to be moved about widely in every direction. Though the operator must be standing at the start (Fig. 5), following the lumen after introduction (*D*, Fig. 4) usually requires him to sit.

Exposure of anterior branches, such as the middle lobe bronchus or the anterior branches of the left upper lobe bronchus, requires lowering of the patient's head and a low position for the operator.

fingers may be acquired by work first in a rubber tube and then in the natural passages of the living dog. This is the only way it can be acquired. It is not only brutal to attempt to acquire it on living human beings without previous practice, but in the latter the stress is so great and the time is so short that little is learned. Just as the pupil in ophthalmology is not given a human being to put blind by an attempt at a cataract operation

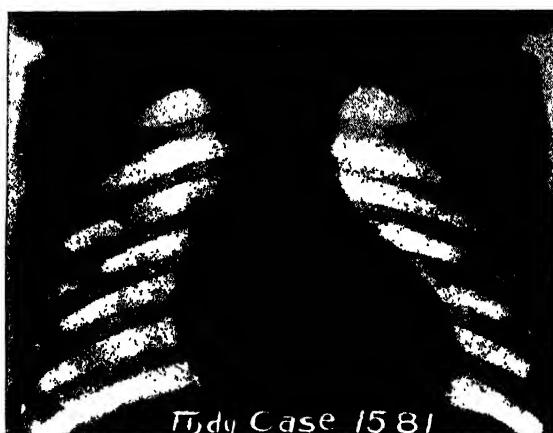


Fig. 8.—Typical example of many cases of overlooked foreign body as a cause of chronic lung suppuration: A girl, aged 4½ years, was supposed for a year and a half, by successive practitioners, to have asthma, asthmatic bronchitis, pulmonary abscess, and tuberculosis for which climatic treatment was advised. The mother insisted on the Roentgen-ray examination that revealed the staple, the bronchoscopic removal of which completely cured the patient. Film by Dr. Willis F. Manges. (Jour. Amer. Med. Assoc.)

Acquiring Skill.—Practice is required to execute the manipulations of introduction of the instruments, and the teaching by a master is almost indispensable. After skill in introduction is acquired, education of the eye to the endoscopic appearances in health and disease is essential for diagnosis. The removal of foreign bodies requires a long period of education of the eyes and the fingers to the peculiar requirements imposed by work through a tube with one eye only. This education of eyes and

without preliminary training on pig's or sheep's eyes obtained from the butcher, just so the pupil in endoscopy should be trained to *see* and to *work by sight*, first in a rubber tube and then on the living dog. All the anatomical landmarks must be learned by bronchoscopy on the cadaver repeated at least 50 times, preferably on a number of different cadavers.

Overlooked Foreign Bodies in the Bronchi and Esophagus.—It is interesting and important to note that of the 1700 cases of foreign body coming

to the Bronchoscopic Clinics, over 200 were cases in which the foreign body had been overlooked for periods of a few weeks to 40 years (Figs. 8, 9, and 10). It seems, therefore, urgently necessary that foreign body be excluded in every case of acute or chronic disease of the lungs.

Prognosis of Foreign Body in the Lung.—If it is allowed to remain,

Prognosis of Foreign Body in the Esophagus.—If the foreign body remains, almost all cases result fatally. Almost 100 per cent. of foreign bodies in the esophagus can be removed through the mouth esophagoscopically. In 800 cases at the Bronchoscopic Clinics it has never yet been necessary to resort to external esophagotomy. Many enormous and jagged dentures

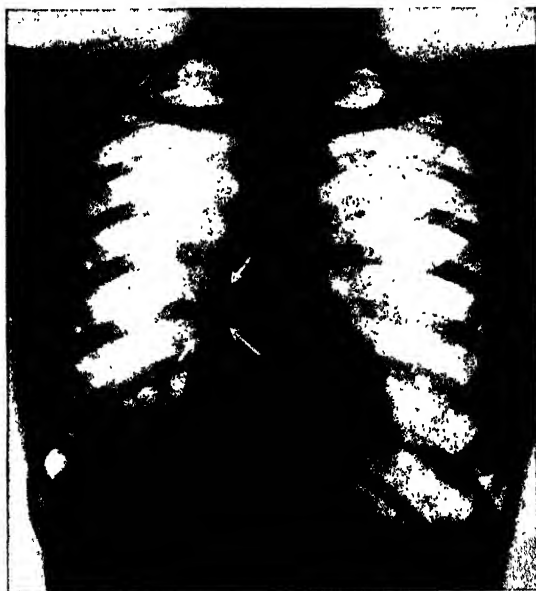


Fig. 9.—(CASE No. Fbdy, 1558.) A roentgenogram of a woman aged 29 years showing the pathological condition in the right lung due to the overlooked presence of a portion of safety pin for a period of fifteen years. Complete recovery followed peroral bronchoscopic removal, notwithstanding 15 years of invalidism. The bronchoscopic removal required only 10 minutes and 18 seconds, and was done without general anesthesia. (Surg., Gyn. and Obst.)

only about 2 or 3 per cent. of the patients recover by coughing up of the foreign body. Peanut kernels and other vegetal substances are usually fatal to babies in a few weeks. Metallic substances, if not completely obstructive, may not prove fatal until after many years of invalidism (Fig. 10). Bronchoscopic removal can be accomplished in almost 100 per cent. of the cases and about 98 per cent. of the patients recover perfect health.

(Fig. 11), bones and other objects have been removed by peroral esophagoscopy.

Arachidic and Other Forms of Vegetal Bronchitis; Peanut Bronchitis.—These are terms given to the violent inflammatory condition set up in the lungs of children by vegetal foreign bodies. From over 400 cases at the Chevalier Jackson Clinics, these conclusions were reached:

1. Vegetal bronchitis is a peculiar and serious type of septic bronchitis

due to the aspiration of vegetal foreign bodies into the lungs, especially of children.

2. The disease is much more frequent than is supposed, because most of the cases are overlooked. About 200 cases have been observed at the Bronchoscopic Clinic. Many other cases have been published in the literature, though the true significance is not noted in the older literature.

4. A positive history of choking and gagging while eating peanuts, peanut candy, or, in fact, any food, followed by cough and wheezing, is diagnostic of a foreign body having entered the tracheobronchial tree. It may or may not have remained there, but it cannot be too strongly emphasized that the disappearance of these symptoms does not mean that the foreign body is not still present in the



Fig. 10.—Roentgenogram of a woman, aged 47, showing a screw that had been in the lung, overlooked by physicians during forty years of invalidism. Notwithstanding the forty years of lung suppuration the patient made a perfect recovery after the bloodless peroral bronchoscopic removal of the screw. This was accomplished under local anesthesia in 7 minutes, 21 seconds. (Surg., Gyn. and Obst.)

3. The chief etiologic factor in vegetal bronchitis is the aspiration into the lower air passages of peanut kernels, nut kernels, beans, watermelon seeds, maize (corn), apple, orange or other fruit seeds or pulp. Foliage, stems, wood fiber or any vegetal substance may cause it. Age is the most important general factor; it is peculiar to children, and severity is usually inversely as the age. Carelessness is usually involved in the etiology.

lower air passages. There is often a symptomless interval, though with the peanut and other vegetal foreign bodies this interval is usually short—a few days or in some cases only a few hours in very young children. When a child, even though symptomless, is brought to a physician with the history of having had an attack of choking, gagging and coughing while eating anything, there is a *prima facie* case; but it is not a question of

innocent till proved guilty. The case should be regarded as one of aspirated foreign body till it has been proved otherwise by all the diagnostic means we possess.

5. Diagnosis is by: (a) The Roentgen-ray evidence of obstructive emphysema or obstructive atelectasis followed later by drowned lung; (b) the physical signs of bronchial obstruction; (c) wheezing or the audible slap heard at the open mouth; (d) history of choking and gagging is important if present, unimportant negatively. In most cases in which there is doubt a diagnostic bronchoscopy should be done.

The subject of diagnosis has been fully discussed elsewhere by McCrae and by Manges.

6. Recoveries may be expected in about 98 per cent. of the cases of children about two years of age with vegetal bronchitis in which the foreign body is bronchoscopically removed within a few days after its entrance. The prognosis is progressively worse directly as the length of sojourn and inversely as the age of the child. With the foreign body unremoved, the cases are all fatal, except in the relatively few instances in which the foreign body is spontaneously expelled.

7. Fully half the cases could be prevented if children without molars were never given peanuts, peanut candy, nut candies or cakes. No child should be allowed to play with corn (maize), beans, peas, coffee berries and the like. All seeds should be removed from watermelons, orange juice, etc., before serving to children.

8. Only one method of treatment is worthy of a moment's consideration; namely, bronchoscopic removal

of the vegetal foreign body and aspiration of the secretions.

BRONCHOSCOPY FOR FOREIGN BODY.—As stated by W. W. Keen, "Bronchoscopy in the hands of . . . has revolutionized the methods of dealing with foreign body in the lung." In the last 500 cases of foreign bodies in the trachea, bronchi and lungs received at the Bronchoscopic Clinic, the foreign body has been removed bronchoscopically through the mouth



Fig. 11.—Large artificial denture impacted in the esophagus of a man aged 28 years. Removed in 2 minutes, 11 seconds, by peroral esophagoscopy without anesthesia, general or local.

in 98 per cent. The total mortality was less than 2 per cent., and in no case was death caused by the insertion of the bronchoscope considered apart from the condition for which it was done.

SYMPTOMATOLOGY OF FOREIGN BODIES IN THE AIR AND FOOD PASSAGES.—The decision as to whether or not a bronchoscopy or an esophagoscopy is indicated depends upon a full understanding of the symptomatology and of the diagnostic steps to be taken. The following

is a résumé of the experience of over 30 years' study of this subject:—

Initial Symptoms.—The most important initial symptoms are choking, gagging, coughing and wheezing, often followed by a symptomless interval. A foreign body may be in the larynx, trachea, bronchi, nasal chambers, nasopharynx, fauces, tonsil, pharynx, hypopharynx, esophagus, stomach, intestinal canal, or may have been passed by bowel, coughed out or spat out, with or without knowledge of the patient. Initial choking, etc., may have escaped notice or may have been forgotten.

Laryngeal Foreign Body.—One or more of the following laryngeal symptoms may be present: Hoarseness, croupy cough, aphonia, odynphagia, hemoptysis, wheezing, dyspnea, cyanosis, apnea, and subjective sensation of foreign body. Croupiness usually means subglottic swelling. Obstructive foreign body may be quickly fatal by laryngeal impaction on aspiration or on abortive bechic expulsion. Lodgment of a non-obstructive foreign body may be followed by a symptomless interval. Direct laryngoscopy for diagnosis is indicated in every child having laryngeal diphtheria without faucial membrane. (No anesthetic, general or local, is required.)

In the presence of laryngeal symptoms the following possibilities should be considered:—

1. A foreign body in the larynx.
2. A foreign body loose or fixed in the trachea.
3. Digital efforts at removal.
4. Instrumentation.
5. Overflow of food into the larynx from esophageal obstruction due to foreign body.
6. Esophagotracheal fistula from

ulceration set up by a foreign body in the esophagus, followed by leakage of food into the air-passages.

7. Laryngeal symptoms may persist from the trauma of a foreign body that has passed on into the deeper air or food passages or that has been coughed or spat out.

8. Laryngeal symptoms (hoarseness, croupiness, etc.) may be due to digital or instrumental efforts at removal of a foreign body that was never present.

9. Laryngeal symptoms may be due to acute or chronic laryngitis, diphtheria, pertussis, infective laryngotracheitis, and many other diseases.

10. Deductive decisions are dangerous.

11. If the Roentgen ray is negative, laryngoscopy—direct in children, indirect in adults—without anesthesia, general or local, is the only way to make a laryngeal diagnosis.

12. Before doing a diagnostic laryngoscopy, preparations should be made for taking a swab-specimen and for bronchoscopy and esophagoscopy.

Tracheal Foreign Body.—(1) "Audible slap" (Jackson); (2) "palpatory thud," and (3) "asthmatoïd wheeze" (Jackson) are pathognomonic. The "tracheal flutter" has been observed by McCrae. Cough, hoarseness, dyspnea and cyanosis are often present. Diagnosis is by Roentgen ray, auscultation, palpation, and bronchoscopy. The "asthmatoïd wheeze" is heard with the ear or stethoscope bell (McCrae) at the patient's open mouth, not at the chest wall. The observer should listen long for the "audible slap," also heard at the open mouth. This is the name given by the author to the peculiar sound caused by the sudden arrest of the foreign body by

the subglottic narrowing, during nature's expiratory or hecic attempt at expulsion of the intruder. When felt by the examiner's thumb on the trachea it constitutes the sign that the author has called the "palpatory thud." History of initial choking, gagging, and wheezing is important if elicited, but is valueless negatively.

Bronchial Foreign Body.—Initial symptoms are coughing, choking, asthmatic wheeze, etc., as noted above. There may be a history of these or of tooth extraction. At once, or after a symptomless interval, cough, blood-streaked sputum, metallic taste, or a special odor of foreign body may be noted. Non-obstructive metallic foreign bodies afford few symptoms and few signs for weeks or months. Obstructive foreign bodies cause atelectasis, drowned lung, and eventually pulmonary abscess. Lobar pneumonia is an exceedingly rare sequel.

Vegetal organic foreign bodies such as peanut kernels, beans, watermelon seeds, and the like cause at once violent laryngotracheobronchitis (*arachidic bronchitis*) with toxemia, cough and irregular fever, the gravity and severity being inversely as the age of the child.

Bones and metallic bodies after months or years produce changes which cause chills, fever, sweats, emaciation, clubbed fingers, incurved nails, cough, foul expectoration, hemoptysis—in fact, all the symptoms of chronic pulmonary sepsis, abscess or bronchiectasis, and many signs which may suggest pulmonary tuberculosis. The apices, however, are normal and bacilli are absent from the sputum.

It must always be borne in mind that a foreign body lodged in the esophagus may present many of the signs

of bronchial foreign body. This is caused in two ways:—

(a) A foreign body in the esophagus, by the obstruction offered to swallowing, may cause foods, liquids and saliva to overflow into the larynx, whence they are inspired into the lungs.

(b) A foreign body lodged in the esophagus may in time ulcerate its way into the trachea, producing a fistula through which food, liquids and saliva leak directly into the lower passages. The symptoms of pulmonary disease are violent in either form, and if the foreign body is not removed, death quickly follows.

DIAGNOSIS.—The Roentgen Ray.—The Roentgen ray is the most valuable diagnostic means; but careful notation of physical signs by an expert is, in all cases, essential. Expert ray work will show all metallic foreign bodies and many of less density, such as natural teeth, bones, shells, buttons, etc. If it is negative, a diagnostic bronchoscopy should be done in all cases of unexplained obstruction.

Peanut kernels, maize, watermelon seeds, and other vegetal substances in the bronchi produce obstructive emphysema of the invaded side. Fluoroscopy shows the diaphragm flattened, depressed, and of less excursion on that side; at the end of expiration, the heart and mediastinal wall move over toward the uninvaded side, and the invaded lung becomes less dense than the uninvaded lung, from trapping of the air by the expiratory, valve-like effect of obliteration of the "forceps spaces" that during inspiration afford air ingress between the foreign body and the swollen bronchial wall. This partial obstruction causes *obstructive* emphy-

sema, which must be distinguished from *compensatory* emphysema, in which the ballooning is in the unobstructed lung, because its fellow is wholly out of function through *complete* "corking" of the main bronchus of the invaded side.

Physical Signs.—Secretions, normal and pathologic, may shift from one lo-

(McCrae) or rarely, a peculiar *râle* or a peculiar auscultatory sound. The most nearly characteristic physical signs are:—

1. Limited expansion.
2. Decreased vocal fremitus.
3. Impaired percussion note.
4. Diminished intensity of breath-sounds distal to the foreign body.



Fig. 12.—Four large, stiff, interlocked safety-pins impacted in the esophagus of a child, aged 9 months. Successfully dealt with by peroral esophagoscopy. (Jour. Amer. Med. Assoc.)

cation to another; the foreign body may change position, admitting more, less, or no air, or it may shift to a new location in the same lung or even in the other lung. A recently inspired pin may produce no signs at all.

The signs of diagnostic importance are chiefly those of partial or complete bronchial obstruction, though a non-obstructive foreign body, *e.g.*, a pin, may cause limited expansion

Complete obstruction of bronchus followed by drowned lung adds absence of vocal resonance and vocal fremitus, thus often leading to an erroneous diagnosis of empyema. Varying grades of tympany are obtained over areas of obstructive or compensatory emphysema. With complete obstruction there may be tympany from collapsed lung for a time.

Râles in case of complete obstruction are usually most intense on the uninvaded side. In partial obstruction they are most often found on the invaded side distal to the foreign body, especially posteriorly, and are often most intense at the site corresponding to that of the foreign body.

A foreign body at the bifurcation of the trachea may give signs in both lungs.

Early in a foreign body case, diminished expansion of one side, with dull-

clude this diagnosis. Bronchial obstruction in pneumonia is exceedingly rare. As stated by McCrae:—

"There is no one description of physical signs which covers all cases. If the student will remember that complete obstruction of a bronchus leads to a shutting off of this area, there should be little difficulty in understanding the signs present. The diagnosis of empyema may be made, but the outline of the area of dullness, the fact that there is no shifting dullness

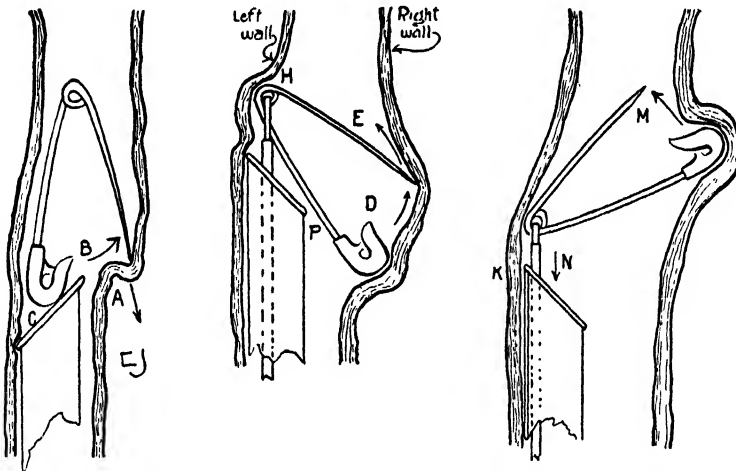


Fig. 13.—Version in the plane of expansion. Advancing the point as indicated by the dart A, which would occur if the keeper C (always the first seen) was pulled on, would result in perforating the esophageal wall at A. Following the author's dictum: "Advancing points perforate; trailing points do not," the point is made to trail as indicated by the darts D and E. This is accomplished with the dull-pointed rotation forceps. Assuming the point of the pin is to the right, strong pressure is made on the left tissue wall as shown at F, overriding the keeper with the tube-mouth, which is passed to the left of the keeper. As soon as the ring of the spring H comes into view the dull points of the rotation forceps are closed into it. Still bearing strongly to the left, as at K, traction made in the direction of the dart N will rotate the pin, causing the point to trail, as at M. Sometimes it is necessary to start the version in the desired direction by a little counterpressure with the tube-mouth P. Sometimes the jaws are passed down over the keeper branch, but usually the ring is exposed and grasped as here shown. It is sometimes advantageous to go anterior or posterior to the keeper in getting an exposure of the ring of the spring. This method is sometimes used fluoroscopically; it is a dangerous procedure—exceedingly so unless the double-plane fluoroscope be used. (*Arch. of Otolaryngol.*)

ness, may suggest pneumonia in the affected side; but the decreased vocal fremitus and the diminished breath sounds with absence of or decreased vocal resonance and absence of typical tubular breathing should soon ex-

and the greater resistance which is present in empyema nearly always clear up any difficulty promptly. The absence of the frequent change in the voice sounds, so significant in an early small empyema, is of value. A large

empyema should give no difficulty. If difficulty remains, the use of the needle should be sufficient. In thickened pleura, vocal fremitus is not entirely absent, and the breath sounds can usually be heard, even if diminished. In case of partial obstruction of a bronchus, it is evident that air will still be present, hence the dullness may be only slight. The presence of air and secretion will probably result in the breath sounds being somewhat harsh, and will cause a great variety of râles, principally coarse,

sense of a foreign body, constant or, more often, on swallowing. Odynphagia and dysphagia or aphagia may or may not be present. Hematemesis and fever may occur from the foreign body or from rough instrumentation. Symptoms referable to the air-passages may be present owing to: (1) Overflow of secretions on attempts to swallow through the obstructed esophagus; (2) erosion of the foreign body through from the esophagus into the trachea; (3) compression of the trachea by a large foreign body in the

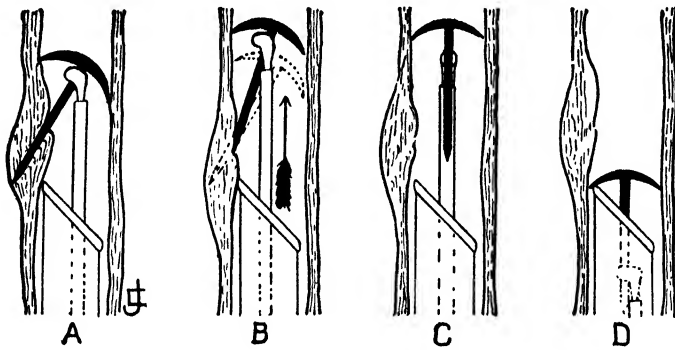


Fig. 14.—Problem of the upholstery tack with buried point. If pulled upon, the imminent perforation of the mediastinum, as shown at A, will be completed, the bronchus will be torn, and death will follow even if the tack be removed, which is of doubtful possibility. The proper method is gently to close the side-curved forceps on the shank of the tack near the head, and push downward as shown by the dart in B, until the point emerges. Then the forceps are rotated to bring the point of the tack away from the bronchial wall. (From "Peroral Endoscopy;" also "Bronchoscopy and Esophagoscopy," W. B. Saunders Co.)

and many of them bubbling. Difficulty may be caused by signs in the other lung or in a lobe other than the one affected by the foreign body. If it is remembered that these signs are likely to be only on auscultation, and to consist largely in the presence of râles, while the signs in the area supplied by the affected bronchus will include those on inspection, palpation and percussion, there should be little difficulty."

Esophageal Foreign Body.—After initial choking and gagging, or without these, there may be a subjective

esophagus, or (4) trauma inflicted on the larynx during attempts at removal, digital or instrumental, the foreign body still being present or not.

The diagnosis is made by the Roentgen ray, first without, then, if necessary, with a capsule filled with an opaque mixture. Flat objects, such as coins, always lie with their greatest diameter in the coronal plane of the body, when in the esophagus; in the sagittal plane, when in the trachea. Lateral, anteroposterior, and sometimes also quartering roentgenograms are necessary.

MECHANICAL PROBLEMS OF BRONCHOSCOPIC AND ESOPHAGOSCOPIC REMOVAL OF FOREIGN BODIES FROM THE AIR AND FOOD PASSAGES.—While the introduction

of the bronchoscope or esophagoscope is easily learned by anyone who will devote the necessary time to it under a competent teacher, in foreign body cases there is involved in addition, in most instances, a mechanical problem in the seizure, version, disentanglement or disimpaction of a foreign body. This problem may be easily

realize the danger of pulling upon a foreign body. This is particularly true of pins, needles, safety-pins, tacks, staples, pointed, sharp, rough, curved or bent foreign bodies. Many hours of practice with a duplicate of the foreign body in a rubber tube and in the living moving bronchi of a dog are essential not only to removal but to avoidance of disaster. The extreme difficulties encountered and the fact that these difficulties may be successfully dealt with by careful working

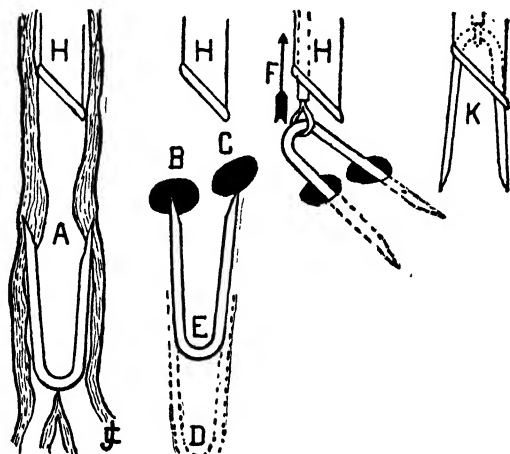


Fig. 15.—Schema illustrating cephalic version of bronchially-lodged staples or double-pointed tacks: *H*, bronchoscope. *A*, swollen mucosa, covering points of staple. At *E*, the staple has been manipulated upward with bronchoscopic lip and hooks until the points are opposite the branch bronchial orifices, *B*, *C*. Traction being made in the direction of the dart, *F*, by means of the rotation forceps, and counterpressure being made with the bronchoscopic lip on the points of the staple, the points enter the branch bronchi and permit the staple to be turned over and removed with points trailing harmlessly behind, *K*. There are about five other ways of dealing with the staple, the best of which is by covering the points with forceps and then sliding the bronchoscope down over them. (From "Peroral Endoscopy"; also "Bronchoscopy and Esophagoscopy," W. B. Saunders Co.)

solved, or may present great difficulty, unless known beforehand and properly worked out on the manikin board.

To grasp a foreign body and pull upon it will, with many kinds of foreign bodies, not only not succeed in removing the foreign body, but will make removal a more difficult matter and may kill the patient. Many deaths have resulted from failure to

upon the problems were demonstrated in the case illustrated in Fig. 12.

The small esophagoscope required in babies (only 9 months old in the case just referred to) enormously increases the difficulties. The extent to which the solution of the mechanical problems of safe bronchoscopic removal of foreign bodies has been worked out will be realized from the fact that

there are sixteen methods of peroral bronchoscopic removal of safety-pins, one of which is illustrated in Fig. 13. In Figs. 14 and 15 are shown the solutions of other problems.

BRONCHOSCOPY FOR DISEASE.—The earliest use of the bronchoscope was for the removal of foreign bodies from the lungs. During recent years, however, bronchoscopy

scope is absolutely invaluable, and in many cases is the only means by which a positive diagnosis can be made. It has been noted in all regions of the body now locally examined that inferential diagnosis was satisfactory until methods of local examination demonstrated that the satisfaction was a matter of misplaced confidence and that the diagnosis had generally



Fig. 16.—Pneumonogram of the living patient, showing the value of pneumonography in outlining bronchiectatic conditions. The contrast with the pneumonogram, Fig. 17, showing normal bronchi, is very striking. Dry bismuth subcarbonate was insufflated bronchoscopically by Dr. Louis H. Clerf. Film by Dr. Willis F. Manges. (Jour. Amer. Med. Assoc.)

for the diagnosis and treatment of disease has become an invaluable aid to the surgeon, the internist, and the pediatrician.

Bronchoscopy is sometimes required to determine the mere presence or absence of suppuration in pulmonary disease; but for the purpose of differential diagnosis as to chronic bronchitis, abscess, bronchiectasis, bronchiectatic abscess, spirochetosis, neoplasms, bronchial stenosis (Fig. 21) and other conditions, the broncho-

scopy has been wrong; in other words, local examination has revolutionized diagnosis and treatment. Bronchoscopy has done this in the matter of foreign bodies and is doing it in respect of a number of other conditions. An accurate diagnosis as to the exact location and especially as to the character of the lesion is fundamental in any scientific method of treatment of any disease. These local conditions in pulmonary disease can be determined bronchoscopically with great accuracy

and with all the certainty of direct inspection.

Specimens of Secretions.—Sputum is unobtainable or obtained with difficulty in very young children. Even when obtained in children or adults, it is so contaminated with oral secretions as to render untrustworthy any investigations or any vaccines made from it. On the contrary, when secretions are obtained bronchoscopically,

colleagues. (Fig. 18.) There are many advantages in using the bronchoscope for pneumonographic insufflation or instillation of the opaque substance selected for the particular case.

Hemoptysis.—In all cases of supposed tuberculosis unconfirmed by the presence of tubercle bacilli in the sputum there is an indication for a diagnostic bronchoscopy to determine



Fig. 17.—Pneumonogram by the Jackson method of bronchoscopic bismuth insufflation for the localization of the bronchi in reference to a small fragment. The bronchi are normal in shape and distribution, affording a graphic basis for comparison of bronchiectatic bronchi (Fig. 16). Film by Dr. Leon Solis-Cohen. (Jour. Amer. Med. Assoc.)

they are not only uncontaminated but they are taken with great precision from the lesion itself.

Bronchoscopic Pneumonography.—The bronchoscopic insufflation of *bismuth subcarbonate* will render any part of the tracheobronchial tree opaque to the ray. (Figs. 16 and 17.) In some cases it is preferable to use, by bronchoscopic instillation, a few cubic centimeters of *lipiodol*, a form of opaque iodized oil discovered by our French

by direct inspection the source of the blood. Every bronchoscopic clinic is familiar with cases of supposed tuberculosis in which the source of blood was found at diagnostic bronchoscopy to be engorged tracheal capillaries, localized bronchitis, Vincent's bronchitis, spirochetosis, gummata, angioma, papilloma, or other growths, benign or malignant.

Bronchial Obstruction.—Any form of obstruction to the ventilation and

normal upward drainage by ciliary and bechic action will certainly end in chronic suppuration. The diagnosis as to the nature of the obstruction can be made by bronchoscopy through the mouth, without anesthesia, general or local, in a few minutes, and

ismal compressions and malignant involvement, bronchoscopic dilatation or removal is easily done and usually is indicated.

Even in cases with malignant disease (*q.v.*), remarkable results have been accomplished.



Fig. 18.—Bronchoscopic pneumonogram of a man, aged 25 years. This case illustrates the advantages of bronchoscopy for (a) pneumonography, (b) diagnosis, and (c) treatment. At diagnostic bronchoscopy Gabriel Tucker found the left lower lobe bronchus completely "corked" by a plug of inspissated gummy secretion that would have prevented the entrance of an opaque material for pneumonography. Bronchoscopic removal of the "cork" rendered possible the making of the pneumonogram here shown, and eight subsequent bronchoscopic aspirations of pus cured the patient, who was still well 4 months after discharge. Patient from service of Dr. Alfred Stengel.

usually with great accuracy. When a bronchus is obstructed by a foreign body, stricture or web (Fig. 21), granulation tissue, thick pus, or membrane, bronchoscopy is the only method of treatment worthy of a moment's consideration. Except in cases of aneur-

Postoperative Massive Collapse of the Lung.—This is in most cases an atelectasis due to obstruction of a bronchus by thick mucus, the bronchoscopic aspiration of which will quickly cure the patient, as shown by Lee and by Tucker.

Stagnation.—The natural physiologic drainage of the lung is by cough and ciliary action. Our investigations at the Bronchoscopic Clinic indicate that, when an acute infective process has been followed by a subacute condition and this, in turn, is in process of drifting into chronic suppuration, there is stagnation of pus and secretions in the affected portion of the lung. This will soon result in de-

ally a prompt cure follows. We feel that in these subacute cases, especially, bronchoscopic aspiration, by taking the load off the cilia at a critical time, will be a large factor in the prevention of chronic bronchitis, bronchiectasis, and chronic abscess. (Fig. 19.)

Bronchoscopic Aspiration.—This can be carried out by bronchoscopy through the mouth in a few minutes without any anesthetic, general or

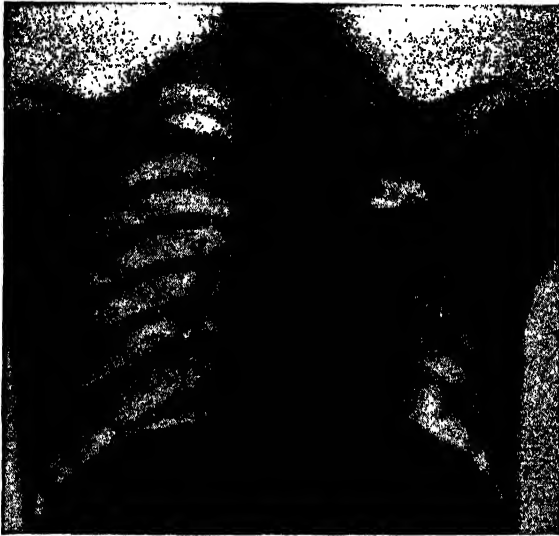


Fig. 19.—Fluid level in a pulmonary abscess, as developed three weeks after tonsillectomy, in a boy aged 9 years. Film by Dr. H. K. Pancoast. (Jour. Amer. Med. Assoc.)

struction of cilia and pathologic changes, first in the mucosa, then in the bronchial walls and alveoli. When, in such a case, after the patient has coughed and coughed until he can get no more sputum up, we go down with a bronchoscope and find foul, discolored pus, we feel justified in saying there is stagnation. In spite of the cough, the pus has remained long enough for the saprophytes to decompose it and for the chromogenic bacteria to discolor it. When we relieve this stagnation by bronchoscopic aspiration, the odor disappears and usu-

ally a sedative may be used or not, as preferred. The bronchoscope has an aspirating canal in the wall of the tube; but more often, in children especially, the independent aspirating tube is preferred. Often both are used. The independent tube (V2, Fig. 1) can be accurately inserted into small bronchi and fistulæ, even at the periphery of the lung, if necessary. Bronchoscopic aspiration is of great aid in the treatment of all forms of lung suppuration.

Bronchiectasis.—Thomas McCrae, who has, from the broadest viewpoint

of internal medicine, seen so much of bronchoscopy, states that "bronchoscopy is of great value in the treatment of bronchiectasis if used early; but *early* should be stressed." This means prompt diagnosis, which is very rarely done. We may be able to prevent advanced bronchiectasis by early recognition and prompt bronchoscopic treatment.

Post-Tonsillectomic Abscess of the Lung.—Etiologically, the evidence

tion; but it is not generally realized that a foreign body lodged in the esophagus can cause serious and even fatal suppurative disease of the lungs. Forty-eight cases of serious degrees of the chronic forms of pulmonary suppuration, due to overlooked foreign body in the esophagus, have come to the Clinic, two of them too late to save life. In the earlier stages the lung suppuration is secondary to inspired overflow reaching the larynx because food and secretions can-

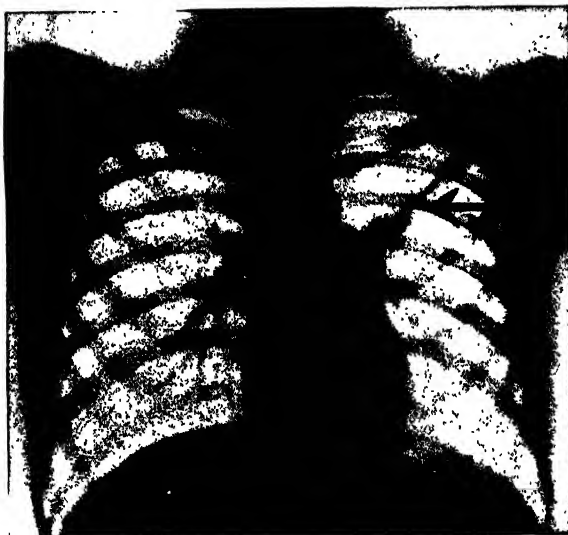


Fig. 20.—Same patient as in Fig. 19. The abscess has healed. Cough, expectoration and all other symptoms disappeared after ten bronchoscopic aspirations by Dr. Gabriel Tucker. Six months later, patient remained entirely well. This case is typical of many in the experience of almost all bronchoscopists. (Jour. Amer. Med. Assoc.)

points strongly to embolism rather than to inspiration as the most frequent channel by which infective materials reach the lungs. Nevertheless, the important clinical fact remains that bronchoscopic aspiration will cure most of these cases if done early in the case (Fig. 20).

Foreign Body or Other Obstruction in the Esophagus as a Cause of Chronic Pulmonary Suppuration.—It is obvious that a foreign body inspired into the bronchi can cause lung suppura-

tion; but it is not generally realized that a foreign body lodged in the esophagus can cause serious and even fatal suppurative disease of the lungs. Forty-eight cases of serious degrees of the chronic forms of pulmonary suppuration, due to overlooked foreign body in the esophagus, have come to the Clinic, two of them too late to save life. In the earlier stages the lung suppuration is secondary to inspired overflow reaching the larynx because food and secretions can-

not readily get down past the foreign body obstruction in the esophagus; later, the suppuration may be secondary to ulceration through into the trachea or bronchus.

The most frequent cause of death in untreated patients with esophageal stricture following lye-burns is bronchopneumonia from inspiration of secretions that cannot normally drain away through the esophagus.

Asthma.—Bronchoscopy for diagnosis and treatment should be considered

in every case of asthma, not only because of the complicating secondary infections and the stagnation so efficiently treated with the bronchoscope, but also because of the fact that thirty-seven children, whose symptoms were entirely due to a foreign body and its secondary suppuration, have come to the Clinic after the diagnosis of bronchial asthma had been made by practitioners elsewhere. In one case, four, in another case, five excellent practitioners had concurred in the erroneous diagnosis (Fig. 8). Moreover, the foreign bodies were, in six of the thirty-seven cases, in the esophagus and not in the lower air passages. Hence esophagoscopy is also sometimes indicated in cases tentatively diagnosed asthma. It is the opinion of pediatricians and internists with whom we have worked that the diagnosis of asthma should not be made in a child without excluding foreign body as a diagnostic possibility by every means at our command. Furthermore, it is now recognized that the asthmatoïd wheeze heard at the open mouth is often a very important diagnostic sign of foreign body.

In addition to the foregoing, we should bear in mind the bronchoscopic discovery of Moore that in certain cases of asthma the most obvious pathologic condition is the presence of thick, tenacious secretion, the bronchoscopic removal of which is often curative.

Vaccine Therapy.—Vaccines obtained from sputum often have little value because of contamination of the specimen. Uncontaminated specimens can be obtained directly from the lesion, by bronchoscopy, in a few minutes, without any anesthetic, general or local. The patient may thus get

all the benefit possible from vaccine methods of treatment.

Congenital Bronchial Stenosis.—This condition is probably not so rare a cause of chronic pulmonary suppuration as the paucity of literature on the subject would seem to indicate. Congenital narrowing of a bronchus does not afford distinctive physical signs or Roentgen-ray evidence of its existence when pathologic sequelæ of obstructed drainage have supervened. Sooner or later congenital narrowings of lumen will give trouble when acute infective bronchial disease has swollen the mucosa sufficiently to obturate the narrow lumen. There are only two means of diagnosis, pneumonography and bronchoscopy. There is only one method of treatment worthy of a moment's consideration, namely, **bronchoscopic dilatation**. This is easily and safely done by a skillful, careful bronchoscopist (Fig. 21.)

Congenital Web of the Bronchus.—While this condition cannot be said to be a common cause of chronic pulmonary suppuration, it is perhaps more common than the literature of the subject would indicate. The only method by which a positive diagnosis of web can be made is with the bronchoscope. In the three cases seen at the Bronchoscopic Clinic, the patients came because of a suspicion of foreign body.

Cicatrical Stenosis of a Bronchus.—Whether due to traumatic, inflammatory, tuberculous, or syphilitic disease, this is quite amenable to **bronchoscopic dilatation**. Bronchial stenosis is an exceedingly rare sequel of foreign body even after years of lodgment and suppuration; almost all cases recover after bronchoscopic removal of the foreign body and fresh

air treatment. About 1 per cent. require dilatation and aspiration for a time.

Benign growths in the lumen of a bronchus cause atelectasis and supuration. They can be diagnosticated only with the bronchoscope (Willy Meyer). **Bronchoscopic removal** causes prompt subsidence of the supuration, which has been due to obstructed drainage and aëration.

has begun in the parenchyma, the diagnosis may not be quite so early, but early enough to give the surgeon a good chance to cure the patient by lobectomy.

Pleuroscopy is done through the chest wall for the removal of lost drains, the breaking up of adhesions, the locating of pockets, and the improving of drainage. For pleuroscopy through a fistula, the pleuroscope or

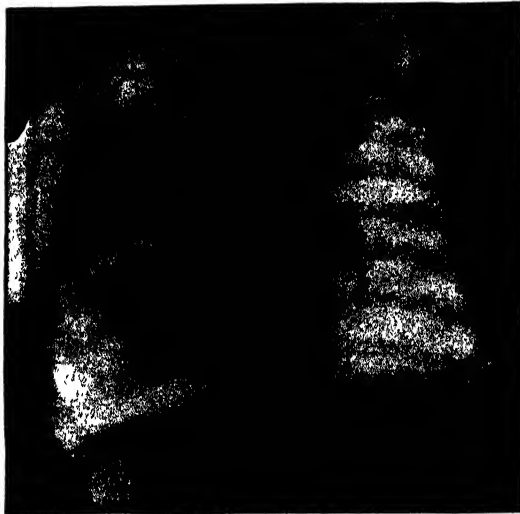


Fig. 21.—Bronchoscopic dilatation of a congenital web-stenosis of the left main bronchial orifice that was the cause of suppurative disease of the left lung. A number of bronchoscopic dilatations resulted in complete cure. Film by Dr. Willis F. Manges. (Jour. Amer. Med. Assoc.)

Malignant Disease of the Lung.—

In malignant disease of the lung, the bronchoscope has brought to the aid of the surgeon an absolute certainty of diagnosis not otherwise possible; and what is even more important, this absolutely certain diagnosis can usually be made at such an early stage of the malignant process that there is a chance to cure the patient by **lobectomy**. In the cases starting endobronchially, the diagnosis can be made at the incipience if opportunity for bronchoscopy is afforded. If the growth

a retrograde gastroscope may be used; for operative exploration, the laryngoscope (A, Fig. 1) is preferable.

ESOPHAGOSCOPY.

Esophagoscopy is a procedure involving the use of an endoscopic tube that serves as a speculum with which to examine the interior of the esophagus (C1, C2, Fig. 1). It has revolutionized not only the methods of dealing with esophageal foreign bodies, but those of diagnosis and treatment of esophageal disease (Keen, Da Costa). As in every other region of the body

in which direct examination has been developed, the many errors of omission and commission due to inferential diagnosis have been eliminated and a scientific basis for procedure been established.

Introduction of the Esophagoscope.

—The first thing to realize is that if an esophagoscope is simply put into the pharynx and pushed upon it will not go into the esophagus, but into the tissues of the mediastinum. Esophagoscopy is so totally unlike the introduction of a soft rubber stomach tube that the practitioner uninformed of the difference will almost certainly cause perforation with the esophagoscope. It is essential that close attention be given to the following details.

The introduction of the esophagoscope calls for the exact position of the patient previously described (Figs. 3 and 4). Unlike bronchoscopy, the laryngoscope is not used for the introduction of the esophagoscope, though it may be used to expose the cricopharyngeal pinchcock if desired. We always put our eye directly to the esophagoscope. With the esophagoscope vertical, the operator finds the right pyriform sinus by sight, no mandrin or laryngoscope being used. Passing downward, the first obstacle is found, at the bottom of the hypopharynx, in the rigid contraction of the cricopharyngeus muscle. It is necessary to wait for this to relax, but while one is waiting continuous *gentle* advancing pressure must be maintained and at the same time the esophagoscope must be pressed anteriorward by the left thumb, to lift it away from the posterior weak point, where it otherwise is almost certain to perforate. This must be done without lowering the head of the patient. The

"handle" of the esophagoscope is not grasped in the hand. It must be up, by which we know that the lip of the tube-mouth is anterior and away from the danger point.

The general direction of the entire esophagoscope is maintained by aiming for the median line as indicated by the midline of the sternum, notwithstanding the fact that we are starting from one side, in the right pyriform sinus. The opening of the lumen is watched for in the *anterior* part of the field. The relaxation of the cricopharyngeal pinchcock is usually accompanied by a regurgitation of saliva, and the slanted end of the tube-mouth glides over anterior to the relaxing cricopharyngeus muscle.

Exploration of the thoracic esophagus is simply a matter of following the lumen as it opens up ahead, a procedure easy of accomplishment when the head is held in the air, free to be moved in every direction, as indicated above.

At the hiatus esophageus the esophagus goes through the diaphragmatic pinchcock. Just as the rubber tube of a burette is pinched tightly shut by the spring clip known as a pinchcock, just so we have the esophagus pinched together at the hiatus by the crura and the muscular fibers of the diaphragm. The point in the lumen of the esophagus corresponding to this pinchcock closure is found by lowering the patient's head to the right and aiming the esophagoscope (or gastroscope) for the anterior superior spine of the left ilium. Gentle but continuous pressure on the proper place will be rewarded after a few moments of patient waiting by the relaxation of the pinchcock. The opening of the hiatal constriction is usually accom-

panied by a rush of gastric fluid, which will be clear if the stomach is "empty" and normal; otherwise it may be mixed with pus, blood, or food.

Once the hiatus is passed the esophagoscope slips so quickly and easily through the abdominal esophagus that the existence of an abdominal esophagus is not realized. No constriction of any kind, functional or structural, is noticed at the cardia, but only a faint difference in color and a marked difference in the form of the folds. The mucosa of the esophagus is paler than that of the stomach. If difficulty is experienced at the hiatal or cricopharyngeal pinchcocks the filiform (*M*, Fig. 1) may be used carefully through the tube by sight to find the lumen; but this is unnecessary and, unless very carefully done, is unsafe.

The comments on ACQUIRING SKILL made under the head of BRONCHOSCOPY apply with equal force to esophagoscopy.

Peroral Gastroscopy.—Exploration of the explorable area of the stomach is carried out in the collapsed state with the open tube esophagoscope by traversing it upward and downward, moving the tube laterally to a new location at the end of each traverse, as with the mechanical stage of the microscope. If desired, a lens system may be inserted in the open tube and the stomach inflated for inspection. The greatest obstacle to reaching the pylorus, especially in adults, is the forward bulging of the spinal column. In children it is not very difficult to reach the pylorus; we have removed perorally a number of times foreign bodies jammed in it. In either adults or children the pylorus can be manipulated by an assistant over far enough to the left for the gastroscopist to in-

spect the pyloric antrum and the pylorus itself.

Peroral Pyloroscopy.—The pylorus is accessible to the peroral gastro-scope with the aid of an abdominal manipulator. Dr. Manges at the Bronchoscopic Clinic has always been able to bring the pylorus in which a foreign body was impacted over to the mouth of the esophago-gastroscope in the stomach, and the foreign body has been removed by grasping forceps inserted through the peroral gastro-scope.

Retrograde esophagoscopy, gastroscopy, pyloroscopy and duodenoscopy are useful procedures that can be carried out in patients on whom gastrostomy has been necessitated by atresia of the esophagus. In such cases a cure of the esophageal occlusion, unless malignant, is greatly facilitated by the retrograde esophagoscopy. The first portion of the duodenum is accessible to the retrograde gastroscope.

ESOPHAGOSCOPY FOR FOREIGN BODY.—Foreign bodies in the esophagus can be removed through the mouth by esophagoscopy with such a degree of certainty and safety that no other method is worthy of a moment's consideration. Training is necessary for the safe use of the esophagoscope. In over 600 cases at the Bronchoscopic Clinic the foreign body was removed in practically all, without mortality due to the procedure. (For the diagnosis of foreign body in the esophagus see under BRONCHOSCOPY FOR FOREIGN BODY.)

In the esophagoscopic removal of foreign bodies it is well to remember that the esophagus differs from the tracheobronchial tree in not standing open. The cervical esophagus is col-

lapsed; the thoracic esophagus is likewise, during expiration. It is a long, loose, dangling, resilient, redundant, more or less collapsed tube, with thin delicate walls, injury to which is usually fatal. Any attempt to push down a foreign body blindly with a bougie is a procedure attended with such high mortality that it is utterly unjustifiable. The old "blind" instruments such as the bristle probang, the sponge probang, and the Graefe basket are entirely discarded as obsolete and dangerous. (For details of the extraction of various kinds of foreign bodies, see under MECHANICAL PROBLEMS OF BRONCHOSCOPIC AND ESOPHAGOSCOPIC REMOVAL OF FOREIGN BODIES FROM THE AIR AND FOOD PASSAGES, page 243.)

ESOPHAGOSCOPY FOR DISEASES OF THE ESOPHAGUS.—

Direct inspection of the esophagus with the esophagoscope has withdrawn the esophagus from the realm of inferential diagnosis and has placed the subject of esophageal disease on a scientific basis. Many of the errors based on theoretic considerations have been eliminated, and the bougie, which was responsible for the errors and for needless deaths, has been discarded as misleading for diagnosis and dangerous for either diagnosis or treatment.

Symptomatology and Diagnosis of Disease of the Esophagus.—The most common symptom of esophageal disease is dysphagia or difficulty in swallowing. This is usually a late symptom, however, and it is of the utmost importance for the practitioner to be on the alert for the very vague and indefinite complaints of patients, usually attributed erroneously to hysteria. The true "globus hystericus" is due to spasm of the cricopharyngeus mus-

cle, but fully 90 per cent. of the patients supposed to have "globus hystericus" are really suffering from the early manifestations of organic esophageal disease. The diagnosis of "globus hystericus" should never be made until organic disease has been excluded by both the Roentgen ray and the esophagoscope.

Dysphagia, difficulty in swallowing, must be distinguished from *odynphagia*, which refers to painful swallowing, whether difficult or not. *Odynphagia* may be due to pharyngeal or laryngeal disease, as well as to hypopharyngeal or esophageal disease. In fact, the esophagus is not well developed in pain sensation; even cancer of the thoracic esophagus is usually painless.

When a patient states that he has noticed a difficulty or even the slightest hesitation or other abnormality in swallowing, the following diagnostic possibilities should be thought of and a diagnosis should be reached by exclusion:—

Ingluviosis, preventriculosis (so-called "cardiospasm").

Dilatation, diffuse; esophagectasia.

Dilatation, local.

Diverticulum.

Stenosis, congenital.

Stenosis, spasmodic.

Stenosis, inflammatory.

Stenosis, cicatricial.

Stenosis, compressive.

Mediastinal tumor.

Mediastinal abscess.

Mediastinal lymphadenopathy.

Aneurism.

Hypertrophied left auricle.

Pericardial effusion.

Pleural effusion.

Pneumothorax.

Esophagitis, acute.

Esophagitis, chronic.

Ulceration: Esophageal, hypopharyngeal, or laryngeal.

Erosion: Esophageal, hypopharyngeal, or laryngeal.

Trauma: Esophageal, hypopharyngeal, or laryngeal.

Malignant neoplasm: Esophageal or periesophageal.

Benign neoplasm: Esophageal or periesophageal.

Goiter.

Tuberculosis: Esophageal, periesophageal, or laryngeal.

Lues: Esophageal, periesophageal, laryngeal, or central.

Paralysis (bulbar disease, myasthenia gravis, syndrome of Avellis, etc.).

Hysteria.

Antiperistalsis.

Angioneurotic edema.

Actinomycosis.

Varix.

Anomaly.

Foreign body in (a) pharynx; (b) larynx; (c) trachea; (d) esophagus.

The general diseases in the foregoing list are considered elsewhere in this work. They are listed here to call attention to the necessity for their diagnostic exclusion.

Any periesophageal mass may by compression affect the functioning of the esophagus.

"Spasmodic" Stenosis of the Esophagus.—There may be peristaltic contractions in any portion of the esophagus rendered visible by the opaque mixture swallowed during the Roentgen-ray examination with the fluoroscope; but these contractions are momentary and are not sufficient to interfere with swallowing; in fact, they may aid it. They are therefore spasmodic, but not stenotic. There are only two places in the esophagus where stenosis from muscular contraction can occur, *viz.*, at the cricopharyngeal pinchcock and at the hiatal pinchcock. These stenoses are due to external and not esophageal musculature, and they are not truly spasmodic; they are the failures to open of these normally shut passages.

Functional Cricopharyngeal Stenosis.—When the oblique fibers of the inferior constrictor contract, the bolus of food is forced downward; the subjacent orbicular fibers, known as the cricopharyngeal muscle, at this moment should coördinately open. Failure to do so gives rise to inability to start food downward, and the patient is thought to have a spasmodic stenosis because the difficulty is not constant. Esophagoscopy is always required to exclude ulceration, cancer, foreign body, benign neoplasm, and tuberculosis. Tuberculosis of the larynx and hypertrophy of the lingual tonsil require exclusion with the mirror in all cases of dysphagia or odynphagia.

Functional Hiatal Stenosis, Preventriculosis, Ingluviosis, Hiatal Esophagismus, Non-malignant Stenosis of the Lower End of the Esophagus, Cramp of the Diaphragmatic Pinchcock, or "Cardiospasm."—These are all names for a disease characterized by dilatation of the thoracic esophagus with prolonged retention of food, which gradually trickles through into the stomach, resembling the functioning of the ingluvies of birds. Hence the term "ingluviosis." Before the days of the esophagoscope the disease was called "cardiospasm;" but the esophagoscope revealed the fact that the stenosis was not at the cardia and that it was not truly spasmodic. By anatomic, cadaveric and clinical studies Mosher demonstrated that the condition is in many instances an organic stenosis associated with abdominal disease, especially abnormality of the left lobe of the liver.

The esophagoscope in preventriculosis or so-called "cardiospasm" will reveal a dilated esophagus containing stale food, and a white, pasty, furred

coating on the esophageal mucosa. The hiatal pinchcock will yield to gentle, persistent pressure of the esophagoscope, which will then glide into the stomach without resistance. All of this is under the guidance of the eye at the proximal tube-mouth.

The condition is quite curable as to symptoms; but recurrences in a proportion of the cases require repetition of the treatment. The accompanying redundancy of the esophagus never disappears as an anatomical fact.

The passage of the **esophagoscope** of full size will cure some cases; others will require **dilatation of the hiatal esophagus**, esophagoscopic or hydrostatic.

Esophagectasia, or Diffuse Dilatation of the Esophagus.—This is the result of preventriculosis (so-called "cardiospasm"), either present or pre-existent. If the stenosis is still present at the hiatus it should be treated; but the redundancy always remains, even though the patient is symptomless.

Diverticulum of the Esophagus.—This is of two types, pulsion diverticulum and traction diverticulum.

Pulsion diverticulum in a strictly anatomic sense is hypopharyngeal, and not esophageal; but clinically it is best classed as an esophageal disease. It is essentially a hernia of the esophageal wall due to incoördination of the cricopharyngeal pinchcock. The latter is a normal closure due to the tonic contraction of the orbicular or cricopharyngeal fibers of the inferior constrictor; but these fibers normally should relax coördinately to open the pinchcock at the approach of the bolus. Failure to do so results in abnormally great pressure on the hypopharyngeal wall, which herniates as

the result, and practically always at the same point. This point is the triangular space external to the posterior hypopharyngeal wall between the slanting fibers of the inferior constrictor on each side and the orbicular fibers below. The triangular space thus formed constitutes a gap in the support of the hypopharyngeal wall. This wall, like the esophageal wall, is very yielding and elastic; it is dependent on support, and yields where this support is deficient.

The size of the sac increases steadily, rendering swallowing more and more difficult because the sac always fills first before any food can get down the esophagus.

The only cure is surgical; the **Gaub-Jackson** (Fig. 22) is the best operation, yielding 90 per cent. of cures. Recurrences are rare.

Traction diverticulum occurs in the thoracic esophagus, usually as the result of cicatricial retraction after suppuration in the mediastinal glands. It causes symptoms only when associated with an esophagitis or a stenosis below it. In most cases **esophagoscopic dilatation** is curative of symptoms, though the pouch remains.

Chronic Esophagitis.—Chronic inflammation of the esophagus is more common than is generally supposed. The usual symptom is discomfort back of the sternum and pain, dull, aching or sharp, extending through to the back. The esophagoscope is the only means of diagnosis. The most common cause is stenosis and retention of food. The esophagus normally empties itself promptly and is very intolerant of retention. Lactic and other ferments render the retained food additionally irritating. Treatment consists of **dilatation of the subjacent stenosis** and

the administration of **bismuth subnitrate**, in small doses, dry on the tongue at frequent intervals.

Acute Esophagitis.—Acute inflammation of the esophagus occurs occasionally as the result of trauma, as by swallowed bones or other foreign bodies, but in most instances the inflammatory condition is the result of blind instrumentation, especially blind efforts with a bougie to push downward a foreign body that may or may

the best treatment for acute esophagitis without perforation.

Acute Esophagitis from Lye Poisoning.—The most frequent cause of acute esophagitis is the swallowing of corrosive acids or alkalis, especially household lye. These preparations are composed of sodium hydroxide in the hygroscopic form of soda ash. The cauterant action is as nearly instantaneous as contact with a red hot iron would be. The poisonous nature of

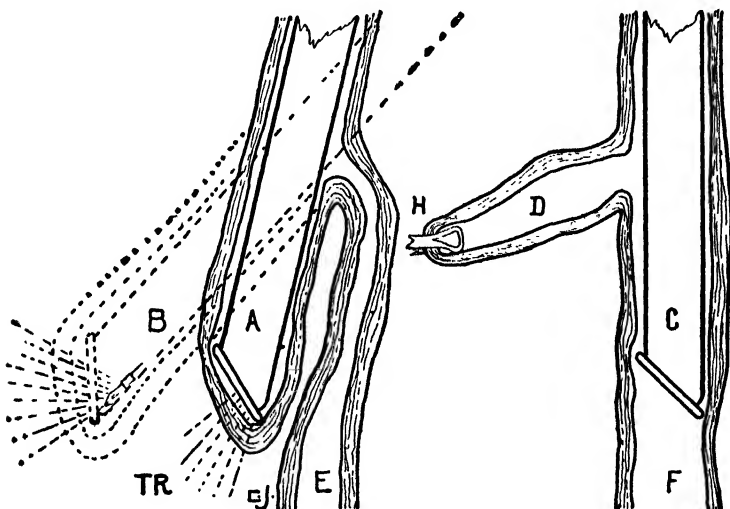


Fig. 22.—Schematic representation of esophagoscopy aid in the excision of a diverticulum: At A the esophagoscope is represented in the bottom of the pouch after the surgeon has cut down to where he can feel the esophagoscope. Transillumination (TR) from the esophagoscopic lamp greatly assists the surgeon in identification and dissection. Then the esophagoscopist causes the pouch to protrude, as shown by the dotted line at B. After the surgeon has dissected the sac entirely loose from its surroundings, traction is made upon the sac, as shown at H, and the esophagoscope is inserted down the lumen of the esophagus, as shown at C. The esophagoscope now occupies the lumen which the patient will need for swallowing. It only remains for the surgeon to remove the redundancy, without risk of removing any of the normal wall. This is known as the Gaub-Jackson operation. (From "Peroral Endoscopy;" also "Bronchoscopy and Esophagoscopy," W. B. Saunders Co.)

not have been present. The prognosis in these cases is bad, and there is no efficient treatment for instrumental perforations but rest of the esophagus. If the esophagitis is due to a foreign body, a prompt cure will follow **esophagoscopy removal**. **Bismuth subnitrate** dry on the tongue in small doses at frequent intervals is

household lye is not realized because its container does not usually bear an adequate "scare" label.

Chemically neutralizing antidotes are **vinegar** or **lemon juice** with plenty of **water**. **Olive oil** is also useful. These remedies, however, must be used immediately to be of any benefit. When the case is seen by the physi-

cian the indications are to **aspirate** obstructive thick **secretions** and to see that the patient gets an abundance of **water**; swallowing is so painful that the patient, usually a child, will refuse water and will soon become dangerously dehydrated. **Bismuth subnitrate**, in small doses dry on the tongue, is the best remedy for the esophagitis. If, later, closure of the esophagus is imminent, the patient should be given a **braided silk cord** to swallow; this should be worn to keep the lumen patulous until treatment of the stenosis can be undertaken. The upper end of the string can be worn through the nose instead of the mouth to prevent its being bitten off. How soon the treatment can be undertaken will depend upon the condition of the esophagus as shown by esophagoscopy. The presence of ulceration or sloughing is no contraindication to the wearing of a string; but if the ulcer is located at the site of the stricture, **dilatation** of the stricture will be fatal unless very slowly and carefully done with the **esophagoscope** under guidance of the eye.

Ulceration of the Esophagus.—Benign non-specific ulceration of the esophagus may result from infective trauma, as with a tooth-brush bristle, a bone, or even hastily eaten bread-crusts or toast. The traumatizing agent may have passed on. Long sojourn of a foreign body is nearly always associated with ulceration at the site of lodgment. This or any other form of stenosis usually results in erosion or ulceration from stagnation of foods. Any of these may result in stricture. Lye burns are by far the most common cause of esophageal ulcer; this form of ulceration is usually deep, slow to heal, and, if allowed to con-

tinue, is usually followed by dense and extensive cicatricial stenosis.

Post-cricoidal ulcer is located at the mouth of the esophagus. It is caused by pressure of the cricoid cartilage backward, pinching the esophageal and hypopharyngeal mucosa between the two hard structures, the spine and the cricoid cartilage. The cricopharyngeal and inferior constrictor muscles do the pulling backward of the cricoid. This is a normal condition; it is only in cases of low vitality in wasting diseases such as typhoid fever that the pressure results in ulcer. It is called decubitus ulcer, but the recumbent posture is not responsible. The weight of the cricoid cartilage is as nothing compared to the constant tonic muscular pull backward of the cricoid. Decubitus ulcer is often followed by cicatricial stricture. At the Bronchoscopic Clinics of Philadelphia, three brothers of one household were treated for this post-typhoid type of stricture. All were cured by **dilatation** by the Gabriel Tucker method.

Peptic ulcer of the esophagus is now known to be more common than was supposed in the pre-esophagoscopic days. It is located in the lower third of the thoracic esophagus. Notwithstanding it is above the hiatus esophageus, it is flooded at times with gastric juice, which seems to be the chief etiologic perpetuating factor, as well as the cause of the pain, extending through to the back. Peptic ulcer leaves dense cicatrices which usually result in stricture. The only method of diagnosis is by esophagoscopy.

Sodium bicarbonate will relieve the pain. Esophagoscopic applications of **silver nitrate** twice weekly will cure the ulcer. **Bismuth subnitrate** dry on the tongue after food or drink

for local effect is a useful adjunct. Rough foods should be avoided.

Tuberculous ulcer of the esophagus is of two types: (1) Erosion and superficial ulceration starting in the mucosa; this is rare. (2) Ulceration through of a broken down tuberculous mediastinal gland; this is not so rare. The superficial type usually heals if the general condition improves, and little, if any, scar is left. The type associated with glandular invasion usually leaves dense cicatrices which may cause stricture or, by forming a band across the esophagus, may cause a diverticulum of the type usually spoken of as "traction," though the mechanism here is not always that of traction. The only means of diagnosis is with the esophagoscope.

The esophagosopic treatment is directed to the prevention of secondary stenosis. General treatment is, of course, very important.

Syphilis of the esophagus exemplifies one of the less common locations for a syphilitic lesion, but such a lesion here is not so rare as was supposed in the pre-esophagosopic days. Mucous plaques are rare, but ulcer from breaking down of a gumma is not rare. The esophagoscope is invaluable for diagnosis and in the prevention of stenosis. If the diagnosis is made late, esophagosopic treatment of cicatricial stenosis will be of utmost importance.

Diagnosis of Ulcer of the Esophagus.—This can be made in only one way, *viz.*, by the esophagoscope. This instrument is, in fact, an esophageal speculum. The Roentgen-ray examination (which should always precede esophagoscopy) may or may not show the ulcer; it will, however, show cica-

tricial narrowing of the lumen if any such post-ulcerative lesion exists. The esophagosopic appearances to the experienced eye are often sufficient to distinguish between the different types of ulcer, but the corroboration of the systemic tests and in some cases biopsy to exclude malignancy are important adjuncts. In many cases at the Bronchoscopic Clinic the patient has come in the agony of despair from a previously made erroneous, inferential diagnosis of cancer. These patients we have been able to send away happy after the cure of benign ulceration. Such cases are important demonstrations of the fact that a diagnosis of esophageal disease ought not to be made without looking at the esophagus.

Treatment of Non-specific Ulcer of the Esophagus.—This consists in restriction of the diet to liquids, not only to avoid the mechanical irritation of solids, but also to obviate the irritation always set up by retention of any food in the esophagus. If there is stenosis, its removal is fundamental to the cure of the ulcer. Silver nitrate and other medicaments may be accurately applied through the esophagoscope. Bismuth subnitrate, dry on the tongue, in small doses at frequent intervals, is the best topical application. When swallowed alone, *i.e.*, without food or drink, it adheres to the ulcerated surface. In some instances gastrostomy may be necessary for stenosis; when thus required it has the additional advantage of putting the esophagus at rest. Post-ulcerative cicatricial stricture calls for esophagosopic treatment (*q.v.*).

Cicatricial Stenosis of the Esophagus.—Such stenosis results from the contraction of the scars left by ulcer-

ation—corrosive, traumatic, post-typhoidal, syphilitic, tuberculous, or peptic. Peroral **esophagoscopic bouginage** with the steel-stemmed filiform (*M*, Fig. 1) is curative in most cases; being done under ocular guidance, it is safe. Blind bouginage is too dangerous to be justifiable. Splitting the esophagus, making a false passage, and other traumata are the inevitable and inevitably fatal results of the blindly passed bougie. Trousseau in the pre-esophagoscopic days said in effect that sooner or later all patients with esophageal stenosis died of the bougie.

Patients with impending death from dehydration should be treated as acidotic and in most of them **gastrostomy** should be done without delay. Of this operation the writer has said: "As with tracheotomy, we always preach doing gastrostomy early, but nearly always do it late." When necessary, gastrostomy has the added advantage that the Gabriel Tucker **retrograde bougie** can be used. This method will cure every case in the shortest possible time consistent with perfect safety. In hundreds of patients we have never seen a death due to its use.

Carcinoma and Sarcoma of the Esophagus.—Sarcoma is rare, but unfortunately cancer is very common. The diagnosis can be made early only with the esophagoscope. The blindly passed bougie often is positively misleading and is inconclusive at best, fatal at worst. The bougie is always negative early because it takes a large well-developed growth to stop a bougie. It is usually negative even late in the sloughing type of growth. If it comes back foul and bloody, the classic inference of cancer is unwarranted:

The odor may be from septic lymphoid tissue; the blood may be from normal mucosa. The history of the case is often equally misleading. The mistake is often made of excluding cancer because of short or long duration of symptoms. It is quite common for the esophagoscope to reveal a cancer in a patient who never had any dysphagia till the day he came in; other patients with cancer have stated that they had trouble in swallowing for 20 years. Intermittent obstruction due to lodgment and subsequent dislodgment downward of food in a cancerous narrowing is commonly mistaken for a spasmodic condition. The Roentgen-ray diagnosis is nearly always correct whether positive or negative, but requires in every case supplementary direct inspection with the esophagoscope.

The lesion as seen through the esophagoscope may be infiltrative, compressive, ulcerative, or may show fungations. A specimen for biopsy may be removed esophagoscopically with safety, and is conclusive.

Cancer of the esophagus is a slowly metastasizing low grade of malignancy, but is almost always fatal because of late diagnosis. When every patient with the slightest abnormality in swallowing is examined at once with the Roentgen ray and the esophagoscope many surgical cures will be possible.

Radium has been disappointing.

Of the palliative measures, **gastrostomy** is always indicated and it should be done early, to put the esophagus at rest. Dilatation is unsurgical, dangerous, and spreads metastases. The most important palliative measure is to see that the patient gets an abundance of **vegetable and fruit juices**,

strained through wire gauze to prevent lodgment. If this be not watched the patient will either suffer from stoppage and stasis or will drift into a depressing, unbalanced diet of milk, raw eggs and meat broths.

Paralysis of the Esophagus.—This condition is usually associated with myasthenia gravis and other bulbar lesions. It is characterized by inability to swallow even liquids, notwithstanding the esophagus is pervious. The esophagoscope shows absence of all normal muscular resistance to its passage. The patient may be fed with a stomach tube. The treatment is that of the condition of the nervous system.

Congenital Anomalies.—Anomalies such as absence of part of the esophagus or an esophagotracheal communication are usually fatal shortly after birth; but a **gastrostomy** is indicated in most cases. If a patulous esophagus all the way to the stomach exists, the patient's life may be saved by surgical closure of the **esophagotracheal fistula**. One patient, 32 years of age, came to the Clinic; she had fed herself for many years with a stomach tube.

Congenital Stenosis of the Esophagus.—This may amount to a complete and fatal atresia, indicated by inability of the newborn child to swallow and by absence of X-ray signs of gas and air in the intestines. Lesser degrees of stenosis become troublesome later when the child begins to try swallowing of solids. The **esophagoscope** is then the means of diagnosis and treatment. Most patients can be thus completely and safely cured.

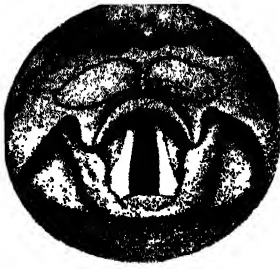
CHEVALIER JACKSON,
Philadelphia.

LARYNX, DISEASES OF. LARYNGITIS.

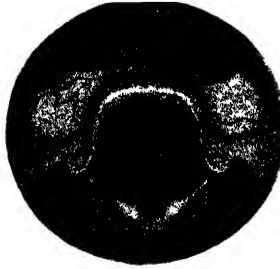
DEFINITION AND VARIETIES.—The term "laryngitis" means inflammation of the larynx; but to distinguish properly the various inflammatory disorders to which this organ is liable, several types of laryngitis are recognized: *Acute laryngitis*, in which the mucous membrane alone is supposed to be inflamed; *edema of the larynx*, in which the deeper tissues become infiltrated; *symptomatic laryngitis*, in which edema and phlegmon may complicate acute laryngitis as a result of microbic infection; *chronic laryngitis*, in which any of the lesions of inflammatory origin observed in the foregoing varieties have assumed chronicity. These types include several disorders to which individual names have been given, but they appear to represent but stages or degrees of the classical forms.

ACUTE LARYNGITIS.

SYMPTOMS.—Acute laryngitis in the majority of cases is the result of the temporary extension of a chronic catarrhal process existing in neighboring tissues, especially the nose, the pharynx, or the tonsils. In professional singers, for instance, constant traveling, with its attending variations in climate and temperature, frequent exposure to dust and smoke, etc., generally keep up a catarrhal disorder of the nasopharyngeal tract. The hyperemia thus induced readily extends by continuity of tissue to the vocal organs under the influence of any undue exposure, dampness, cold, or any factor capable of irritating the laryngeal surfaces. The larynx in such cases may be said to be predisposed to a mild form of catarrh which appears more or less frequently. In



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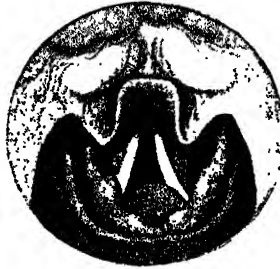
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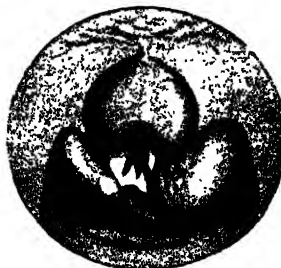
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ISCHEMIC, HYPEREMIC, AND NEOPLASTIC DISORDERS OF THE LARYNX.
(Kreig: Kehlkopfkrankheiten.)

1, anemia of the entire larynx and in particular of the tuberculous infiltration interarytenoid region. Earliest stage. 2, hyperemia of the entire larynx, particularly of the vocal cords. 3, nodular infiltration of the left vocal cord with preservation of the epithelial coat. 4, tumor-like infiltration of the left vocal cord with preservation of the epithelial coat. 5, nodular infiltration on the anterior surface of the posterior wall with intact mucosa. 6, pale infiltration of the posterior wall of the larynx in its entire thickness. 7, nodular infiltrations of the edematous epiglottis and arytenoid regions. 8, nodular infiltration of the edematous arytenoid region. Heart-shaped epiglottis. Swelling with granulations on the posterior wall. 9, nodular infiltration of the inflamed and swollen epiglottis. Arytenoid regions very pale and edematous. Vocal cords ulcerated.

such cases the subjective symptoms mainly consist in a sensation of tickling and soreness or irritation in the larynx, which causes the patient to cough, or produces a constant desire to "hem" and a feeling of constriction at the throat. The voice is altered in quality and pitch, and easily fatigued; it becomes gruff, and hoarseness, more or less marked, follows. Aphonia may even develop. Under the influence of proper treatment and rest the local hyperemia quickly subsides, but the continued use of the voice prolongs the inflammatory process and tends to permanently compromise the integrity of the organ as an instrument.

A laryngoscopic examination sometimes yields but little evidence of inflammation, the interarytenoid space alone showing slight hyperemia. In the vast majority of cases, however, the entire larynx shows congestion, the vocal bands being distinctly red. Much faith cannot be placed upon these signs in the case of male singers, however, the vocal bands being frequently pink and even red in the normal state; but in women, local redness usually means active congestion, unless the patient be addicted to excessive use of alcoholic drinks.

In persons in whom the voice is not subjected to more than ordinary uses an attack of acute rhinitis frequently precedes the laryngeal disorder. When, however, the laryngitis is primary, hoarseness usually occurs as the first symptom, though slight chilliness occasionally alluded to is a premonitory sign. The voice is lowered in pitch; a pricking sensation is experienced in the larynx, which causes hacking and aggravation of

the local congestion. There are usually some cough, slight dyspnea, and occasionally pain during deglutition and a slight rise of temperature. The mucosa is at first very dry, the dryness lasting from one to several days. Expectoration then becomes established and is thin and scanty, later jelly-like and viscid, and still later muco-purulent, and more copious. Hoarseness in the early stages is due to dryness of the mucosa, later to infiltration and thickening of the cords which result in a paresis of their delicate movements.

Laryngoscopically the larynx is found markedly congested, either diffusely or merely in the vocal bands and intra-arytenoid tissues.

Some cases of acute laryngitis are attended by hemorrhagic symptoms, the expectoration of blood usually following violent coughing. Besides the usual laryngeal manifestations, there is generally to be found a circumscribed patch, the seat of rupture of a superficial vessel. In some cases there is no expectoration of blood, but the vocal bands show a red spot of localized hemorrhagic infiltration. It sometimes shows itself independent of a catarrhal condition as a result of undue strain in using the voice. It is probable, however, that a latent catarrhal process is always present in such cases, and that the vascular walls are inordinately weak. (See colored plate.)

The rheumatic diathesis predisposes to a disorder of the larynx simulating acute laryngitis, but differing from it in that local phenomena are usually less active objectively. The voice is used with difficulty and the pain is sometimes much more severe than that experienced in other

inflammatory disorders. There is dyspnea in the majority of cases.

Rheumatism of the larynx sometimes occurs in conjunction with general rheumatism. It is a serious disorder, particularly in singers; one or both of the cricoarytenoid joints may be involved in the inflammatory process, and permanent hoarseness often results.

ETIOLOGY.—Generally speaking, laryngitis may be said to be due either to conditions causing local congestion by mere overuse or mechanical irritation, by continuity of tissue, or by chemical irritation.

The forms thought to be independent of specific germs are those due to exposure to cold and damp; the inhalation of smoke, especially tobacco smoke in a badly ventilated room; dust, irritating fumes, spices, irritating particles of all sorts, etc. Excessive use of the voice and the ingestion of alcoholic drinks, of hot or overspiced food, are also frequent causative factors.

As already stated, catarrhal diseases of the nose and nasopharynx greatly predispose to acute laryngitis, and the majority of cases witnessed show such a condition as a primary factor. Singers, army officers, ministers, etc., are especially prone to this disorder on this account, particularly when the voice is improperly used; but the presence of a primary catarrhal disorder of the nasopharyngeal tract may usually be discerned. Obstructive lesions within the nose, necessitating mouth breathing, may directly or indirectly be the causal agents. Cases are recorded in which the application of remedial agents to the pharynx has been followed by an attack of acute laryngitis produced

by the inhalation of the powder or liquid into the larynx. Irregularities of the gastrointestinal tract, especially in children, may be a predisposing factor. Men appear more susceptible to laryngeal irritation than women, doubtless because they are more readily exposed to professional and trade injuries and indulge to a greater extent in the abuse of alcohol.

PATHOLOGY.—In the idiopathic form of acute laryngitis the superficial vascular supply is mainly at fault and there are very few cases in which a certain amount of cellular infiltration does not occur, and the line of separation between the superficial and deeper changes is not easily discerned. The primary factor in such cases is probably vasomotor, and if the paresis of the vascular nerves is marked the serous infiltration by diapedesis into the tissues may be such as to give rise to slight tumefaction. The epithelium may be softened and, localized desquamation occurring, diminutive erosions are sometimes found.

Acute subglottic laryngitis (laryngitis acuta subglottica) is met with mostly in children, and may occasionally give rise to nocturnal attacks of stenotic dyspnea. The inflammation is here limited to the under surface of the vocal cords, and the swelling of the subglottic tissue may be sufficient to cause it to project beyond the borders of the cords.

TREATMENT.—The patient should be in a warm, moist room, refrain from talking and smoking, and not allow others to smoke around him. Hot food increases the local congestion, and especially the hot alcoholic drinks so frequently indulged in. Cracked ice and ice-cream

are usually grateful to the patient and beneficial to his throat.

An acute attack of laryngitis due to "cold" may often be arrested by the early internal use of potassium bromide and opium. Twenty grains of the former, with 2 drams of paregoric, repeated every three hours, usually reduces the laryngeal hyperesthesia which lies at the bottom of the local symptoms to a minimum, while the likelihood of any complication is greatly decreased. The somnolence also induced tends to reduce the localized congestion. After this effect is obtained, the dose may be reduced by half and taken every two hours, two or three times. A bottle of citrate of magnesia taken the next morning often brings on the stage of resolution. This may be encouraged by means of the compound guaiac lozenges.

In some cases the inhalation of steam impregnated with the compound tincture of guaiac is quite effective, but not nearly as much so as the method given above, which it is calculated to replace when patient cannot take the bromides. One teaspoonful of the compound tincture is placed in a pitcher of water no hotter than the hand will stand comfortably for 10 seconds; the vessel is covered with a towel folded into the shape of a cone; the mouth and nose are inserted into the open top of the cone, and the steam is inhaled deeply as long as it is emitted.

A simple and effective inhaler may be made as follows: Take a pint or quart bottle with a wide mouth; place a cork or rubber stopper in the neck; bore 2 holes a quarter of an inch wide in the stopper; in 1 of the holes place a piece of glass tubing which reaches from a little above the stopper to within a half inch of the

bottom of the bottle; in the other hole place another piece of glass tubing reaching a quarter of an inch below the bottom of the stopper and extending upward for about 10 inches and bent at an angle of about 45 degrees at a point a short distance above the top of the stopper. In the bottle put enough warm, but not hot, water to a measure of $\frac{1}{4}$ or $\frac{1}{8}$ the capacity of the bottle. Pour into the water $\frac{1}{2}$ to 1 teaspoonful of the following:

R *Mentholis* gr. v (0.3 Gm.).

Tr. benzoin, co. ʒj (30 c.c.).

M.

Inhale by drawing through the bent glass tubing and exhale through the nose. These inhalations should be practiced for 5 or 10 minutes every hour or two. The patient should remain indoors, unless the weather be warm, for at least 1 hour after each inhalation; provided, of course, that his local or general condition does not confine him to his home altogether.—[Hitschler.]

In the early stages of acute laryngitis, especially when the mucosa is dry, and indeed well into the period when secretion has become established, the following prescription, as recommended by Freeman, is most efficacious:

℞ *Apomorphinæ* hy-
drochloridi

(0.032-0.065 Gm.),

Sodii citratis 3iv-vi (16 to 24 Gm.).

Succi limonis,

Syrupiāā f3vj (24 c.c.).

Aquæ, q. s. ad ... f̄ij (90 c.c.).

M. et Sig.: Two teaspoonfuls with water every 4 hours. Dispense in amber or blue bottle.

Relief is usually experienced within 12 hours.

The inhalation of steam charged with the compound tincture of benzoin is preferred by some clinicians. It may be employed in the same manner as the tincture of guaiac. The addition of a teaspoonful of paregoric frequently assists the benzoin in relieving the irritation.

In many cases the local disorder is greatly influenced by general disorders. In female professionals, especially, constipation is almost the rule, owing probably to their irregular mode of living, their varying diet, and the continued traveling in railroad cars. Purgatives, even mild aperients, are, for obvious reasons, out of the question when evening after evening the sufferer is to appear upon the stage. **Enemata**, while immediately effective, present the advantage of not diminishing the patient's strength. An enema composed of 1 pint of **lukewarm water** and a tablespoonful of **glycerin** will sometimes be found to act surprisingly, not only on the intestines, but on the voice, especially if, as is often the case with traveling artists, the bowels have not been moved for several days. If fever is present, drop doses hourly of **tincture of aconite** will usually reduce it markedly. If the inflammatory process is in the early stages and the patient's occupation demands the continued use of the voice, Kyle advocated the administration every hour for 3 or 4 doses of a tablet containing:

℞ *Acidi nitrici diluti*,
Tinctura opii .āā ℥iij (0.18 c.c.).
Cocaina phenatis gr. ⅓ (0.006 Gm.).
 Ft. tabell. No. j.

In cases in which the bromides and opium cannot be given a solution of **resorcinol** or **alumnol**, 7 grains to the ounce (0.45 Gm. to 30 c.c.), should be used with an atomizer about every two hours the first day, then three times daily. To enable the solution to thoroughly bathe the bands, the voice should be sounded during inhalation, while the fluid is being sprayed in, the bands being thus

brought in and forming a floor, as it were, at the lowest portion of the larynx. When the hoarseness is great, an application with cotton pledget of **carbolyzed iodotannin** or a solution of **ferric chloride**, 20 grains (1.3 Gm.) to the ounce (30 c.c.), causes a sudden contraction of the capillaries, which is effectively maintained by the **resorcinol** solution.

To hasten the process of resolution, a pill composed of 1 grain (0.065 Gm.) of **quinine** and ¼ grain (0.016 Gm.) of **nux vomica** may be administered every two hours the first day, then four times a day. **Suprarenal gland**, 2 grains (0.13 Gm.), with **strychnin**, ⅓ grain (1 milligr.), in a capsule taken after meals is also very helpful.

In the treatment of rheumatic disorders of the larynx local measures are practically useless. **Sodium benzoate** is sometimes quite effectual, 5 grains (0.3 Gm.) being given every three hours. **Sodium salicylate** is the standard remedy when it can be tolerated. (See RHEUMATISM.)

In acute laryngitis, strong astringents, *e.g.*, tannin and cubeb, are not well tolerated. They are too irritating. Chlorate of potash is soothing. The following formulæ are suggestions:

℞ *Phenolis cryst.* gr. j (0.065 Gm.).
Potass. chlorat. gr. x (0.6 Gm.).
Glycerini 3j (4 c.c.).
Aq. q. s. ad 3j (30 c.c.).

M. To be sprayed into larynx *ad libitum*.

The physician may also use a spray of:

℞ *Cocaina hydrochloridi* gr. j (0.065 Gm.).
Antipyrina gr. x (0.6 Gm.).
Glycerini 3j (4 c.c.).
Aq. q. s. ad 3j (30 c.c.).
 M.

Sprays of argyrol or silvol, 10 to 20 per cent., are very soothing and non-irritating. Solutions stronger than this are apt to

clog the atomizer. Finishing the local treatment with a spray of:

R *Mentholis*,

Camphoræãã gr. ss. (0.032 Gm.).

Petrolati liq. ʒj (30 c.c.).

Ol. anisi gtt. j (0.06 c.c.).

is of service.—[Hitschler.]

EDEMA OF THE LARYNX.

Edematous infiltration of the larynx may occur as the result of a simple catarrhal process, of traumatic laryngitis, or as a complication of infectious disorders, proximate or remote.

SYMPTOMS.—The first manifestation may be a chill, soon followed by hoarseness and laryngeal pain. The most prominent symptom experienced almost from the start is a sensation of constriction at the throat and gradually increasing dyspnea, most marked during inspiration. There is also local heat, dryness, and a muffled cough, which the patient aggravates by efforts to rid the surfaces of a supposed secretion. There is increasing huskiness, both inspiration and expiration being finally impeded. In favorable cases there is a gradual decline of all symptoms; but this course is not always observed, and, unless prompt relief is afforded, the patient dies of asphyxia. The temperature is not, as a rule, much above the normal.

The laryngoscopical examination reveals local changes varying with the cause of the edema. When the latter is secondary to acute laryngitis the upper portion of the larynx over which the tissues are comparatively loose is swelled and red or reddish yellow. The epiglottis sometimes appears as a thick cushion, covering two sausage-like bodies under it, the aryepiglottic folds. As the tissues swell, these tend to roll inward,

forming a series of cushions, whose edges gradually approach one another, steadily reducing the lumen of the laryngeal cavity. When the edema is the result of traumatism or contact with corrosive acids, etc., there is great redness and supplemental local lesions. Marked inflammatory swelling also attends the erysipelatous form.

When edema is due to a general disorder, the mucous membrane is, as a rule, paler than when it occurs as a complication of a local inflammatory process.

In edema occurring as a result of the inhalation of steam, fire, caustic vapors, or due to the deglutition of too hot liquids, or of corrosive substances taken accidentally or with suicidal intent, such as carbolic acid, sulphuric acid, etc., the onset of the symptoms is comparatively sudden. Dyspnea and spasm sometimes occur from the start, and all the symptoms of acute laryngitis enumerated are increased in intensity. The gravest local manifestation of laryngeal inflammation, edema, is soon reached. In the majority of cases met with, however, after a series of acute manifestations, momentary dyspnea and laryngeal spasm, etc., which the physician does not, as a rule, witness, the larynx assumes a comparatively normal condition, as far as the patient goes, though, however, the laryngeal structures become infiltrated and after a few hours—sometimes an entire day—the most distressing symptoms appear, and the patient dies asphyxiated, unless relieved. (See colored plate.)

The upper portion of the larynx may show evidence of tissue destruction when such agents as carbolic acid, ammonia, etc., have been used;

but in the majority of cases laryngoscopic examination only reveals intense redness of all the laryngeal tissues, with slight swelling. The active congestion may be localized, this depending upon the causative agency. In laryngitis due to burning fluids the epiglottis may alone be involved, but in the vast majority of cases neighboring pharyngeal tissues, the interarytenoid space, the ventricular bands, and the vocal bands take part in the inflammation.

ETIOLOGY AND PATHOLOGY.

—The edema occurring as a result of simple catarrhal laryngitis is usually brought on by undue exposure to damp, cold air while the body is overheated by exercise, such as dancing, fencing, etc. *Décolleté* gowns, sitting at open windows after dancing, and drinking ice-water, have caused many deaths—credited to heart disease.

Edema of the larynx has also been observed in cases treated with potassium iodide. (See IODINE AND IODIDES).

It is probable that a latent disorder of the larynx is present in such cases. This may have existed before the use of the iodide or occur as a result of the disease—syphilis, for instance—for which the drug has been administered. Lesions of the kidney may mechanically induce laryngeal edema by interfering with the free elimination of fluids, while valvular heart disease may also predispose to it.

Many of the cases of edema of the larynx are thought to be of infectious origin, exposure of the parts to weakening influences of cold, etc., facilitating the entrance of micro-organisms of neighboring inflammatory processes, particularly of the nasopharynx. The base of the tongue, the mouth, and the tonsils are known to

be sources of infection. Inflammatory disorders of the glands of the neck, parotitis, tonsillitis, Ludwig's angina, etc., may thus suddenly be complicated with edema of the larynx and its dangers.

Burning or scalding of the larynx, traumatisms,—such as those induced by the passage of foreign bodies, sharp bones, tacks, inspiration of irritating fluids, or foreign bodies in the esophagus and lodged directly behind the larynx,—etc., may, as stated, also act as etiological factors. Acute thyroiditis at times produces an alarming edema of the glottis, but here a high leucocyte count will be significant, and the condition must not be mistaken for the presence of pus, when prompt surgical interference is required. Even alcohol has been known to produce localized edema. The occurrence of edema of the larynx in any case is in consequence of some structural alteration involving the local venous circulation.

Records of autopsies made under Virchow gave the following results:

In 3887 examinations edema of the larynx was noted 210 times,—149 in men, 40 in women, and 21 in children. Forty-four cases had occurred in regional disease and 166 in systemic disease. Of 5161 patients treated in the clinic for diseases of the throat and nose, between April 1, 1887, and June 1, 1889, there were only 8 with acute edema of the larynx,—7 in men between 21 and 48 years of age and 1 in a woman 58 years of age.

PROGNOSIS.—Edema of the larynx is at times so rapidly fatal that no warning of the oncoming issue is afforded. A patient suffering from slight hoarseness on retiring may thus be found dead next morning. Though

such cases are comparatively rare, they nevertheless show the importance of promptly attending to acute laryngeal maladies. When the iodides are being administered in connection with throat disorders, the larynx should be frequently examined laryngoscopically.

Cases in which the infiltration is localized are obviously less likely to prove mortal than those involving all the tissues. The latter form is that most frequently met with when general disorders—such as scarlet fever, typhoid fever, variola, etc.—act as the primary factor.

TREATMENT.—When edema is present vigorous measures should be adopted when dyspnea becomes evident. Until then, **cracked ice** should be kept in the mouth and **cold-water compresses** applied around the throat. Free **catharsis** with a saline should be early instituted. The patient should be well covered and given a **hot mustard foot-bath**, then immediately placed in bed, but in the sitting posture, and wrapped in blankets—the object being to cause normal diaphoresis. If this cannot be obtained normally, **pilocarpine** should be given hypodermically, or internally if the local manifestations are not marked.

The **bromides** are useful in reducing the local infiltration, and a dose of 20 grains (1.3 Gm.), for an adult, repeated as often as needed, sometimes proves very efficacious.

Tincture of belladonna, 5 drops every hour until its physiological effects become marked, also tends to counteract the infiltration by contracting the laryngeal blood-vessels.

Astringent solutions should only be used in circumscribed edema, a weak solution of **tannin**, **alumnol**, or

resorcinol being valuable in such cases. When the cases can be closely watched, a 10 per cent. solution of **cocaine** applied directly to the larynx causes momentary—though slight—retraction of the tissues, and may thus be advantageously used, especially when surgical measures are to be resorted to: scarification, intubation, or tracheotomy. In some cases, however, it seems to increase the dyspnea.

When the dyspnea becomes urgent, **scarification** of the laryngeal tumefaction is indicated. With the assistance of the laryngeal mirror—held in the left hand—the procedure is quite easy after anesthetizing the laryngeal tissues with a 10 per cent. solution of cocaine. The pocket-case curved bistoury is wrapped in a piece of bandage held in place with thread up to within $\frac{1}{8}$ inch of the tip, to prevent cutting the tongue with edge of the blade. The tongue being drawn out and held by the patient, the epiglottis will generally be seen standing erect, and looking, when much infiltration exists, not unlike a pale cherry. This should not be punctured first, as the patient may refuse a second incision and the first should be the most profitable one to him. The portion playing the most important part in the production of the dyspnea is the aryepiglottic fold, and this can usually be depleted by means of a short incision into its external border, thus causing the blood and serum to flow into the pyriform sinus, instead of into the larynx proper. When the patient is docile, both sides can be scarified and the epiglottis also, care being taken to prick the edges with the point rather than the internal aspect of the laryngeal walls.

When a laryngoscopic mirror is not at hand, the index finger of the left hand should be passed behind the epiglottis and used as guide for the curved bistoury.

At times scarification, even when thoroughly carried out, does not relieve the dyspnea. In that case the lower portion of the larynx and the tissues beneath the vocal bands will probably be found involved in the inflammatory process, when examined laryngoscopically—if seen at all. Under these circumstances either **intubation** or **tracheotomy** must be resorted to. (See INTUBATION and TRACHEOTOMY.)

When laryngitis is due to traumatism and the manifestations are not sufficiently marked to require operative measures, considerable pain is sometimes present; again, the lesion is so exposed that infection may occur, a benign process thus being transformed into a severe one. The most satisfactory results are to be obtained by strict cleanliness through the use of a 5-grain (0.3 Gm.) solution of **borax** applied with the atomizer, the laryngoscopic mirror being employed to properly locate the spray. Two grains (0.13 Gm.) of pure **iodoform** are then applied with the insufflator. This reduces the pain and curtails the infectious process in any form of laryngitis in which these elements prevail.

SYMPTOMATIC LARYNGITIS.

This term is sometimes applied to the laryngeal manifestations occurring in the course of general diseases, and involving, as a rule, the deeper structures. The symptoms vary with the intensity of the local manifestations, and may range from those of a simple laryngeal catarrh to the most

severe edema calling for immediate tracheotomy. Complications of so dangerous a nature are fortunately rarely witnessed.

Measles is usually attended by inflammatory involvement of the larynx. There is hoarseness and sometimes loss of voice, the symptoms, in fact, being quite those of acute laryngitis, including occasionally slight tumefaction.

The laryngoscope reveals a condition similar to that of the skin, the exanthem showing itself more or less clearly. Red spots project from the surface, giving it an irregular appearance. The process of resolution usually progresses without complication. Occasionally, however, edema or ulceration occurs as a complication.

Variola and Varicella.—The laryngeal manifestations of variola are various. In some cases small pustules are observed; these may gradually develop into a necrotic process, leading to perichondritis and even edema. The symptoms are those of acute laryngitis. The intensity of the local disorders varies with the gravity of the general disease, but, as a rule, the course is a benign one.

In varicella laryngeal symptoms are not as frequently observed as in variola, but they sometimes assume as serious proportions. Deglutition, phonation, and respiration may be seriously impaired, the latter resulting mainly from the smallness of the larynx in children.

Scarlet Fever.—In this disorder more or less marked involvement of the larynx is frequent. In the vast majority of cases, however, the cause of the trouble is benign, and resolution occurs along with the general malady. The exceptions inferred may at least

simulate various grave disorders, such as diphtheria and membranous laryngitis. Edematous infiltration is also occasionally witnessed, and likewise constitutes a grave complication. In all these disorders the tendency to ulceration is markedly increased, and, when this starts, it is checked with difficulty. Perichondritis and hemorrhage owing to destruction of blood-vessels are always to be feared in such cases.

Erysipelas.—There is a form of acute laryngitis closely associated with, if not an actual manifestation of, *erysipelas* of the larynx. This is a dangerous form, and may range from a simple redness to gangrenous changes of the structures. It is often accompanied by edema, high fever, great hoarseness, and dyspnea almost from the start.

Typhoid Fever.—The laryngeal complications of typhoid are to a certain degree typical in the fact that they are circumscribed in the great majority of cases. The parts that most frequently show erosions are the laryngeal surface of the epiglottis near the edge, the ventricular bands, and the upper part of the arytenoid space, the specific character of the complication being thus readily shown. The various ulcerative processes noted in scarlet fever are also occasionally observed in typhoid fever, the tendency to spread being equally marked. The destructive process may not only present itself during the progress of the general affection, but at some time after.

Pertussis.—In whooping-cough the laryngeal manifestations are sometimes quite marked, but they are not attended, as in other diseases, by ulcerative processes. The severe

cough induced occasionally causes marked congestion of the interarytenoid space, accompanied, at times, by extravasation and localized hemorrhage. Slight edema is frequently observed. Diphtheria as a complication has been witnessed, though very rarely. The most annoying feature in connection with the larynx is a resulting hyperesthesia of the interarytenoid space, which may persist indefinitely, the patient being subject to exacerbations of coughing when using his larynx any length of time. A dry, warm, or dusty atmosphere is also likely to cause considerable inconvenience. This sequel is especially apt to occur in adults.

Influenza.—The laryngeal complications of influenza generally occur in the cases in which symptoms affecting the upper respiratory tract are observed. There is the tendency to hemorrhage; ulceration is also occasionally observed. Spasmodic cough is also present, causing considerable distress to the patient by greatly increasing the intensity of the frontal cephalalgia. Edema of the larynx is occasionally met with, but, as a rule, it does not assume grave proportions.

Typhus Fever.—In this disease the manifestations are similar to those in typhoid fever and the complications are also liability to ulceration, edema, or pseudodiphtheria.

Schuch includes under the name of **laryngitis exudativa** a series of affections of the laryngeal mucous membrane in which there is exudation with more or less fluid contained in vesicles or bullæ, or hyperemia with swelling. In **miliaria** there are vesicles on the epiglottis and aryepiglottic folds, giving rise to the sensation of a foreign body. **Herpes** very sel-

dom occurs alone in the larynx; there is usually an implication of skin or of mucous membrane. The vesicles rupture so quickly that they are seldom seen in the first stage, but are usually observed as erosions or small ulcers following the rupture. The contents of the vesicles may be serous, purulent, or even hemorrhagic.

Hoarseness, dysphagia, and pain on swallowing are usually the attendant symptoms, but sometimes nothing but a sensation of soreness is noted.

Schech also groups under the same head **foot-and-mouth disease** (stomatitis epidemica) accompanied by more or less constitutional disturbance and by vesicles in the larynx, which break down into ulcers; **aphthæ**, which sometimes occur in the larynx in association with aphthæ of the mouth or vulva; **pemphigus**, which occasionally forms exudative swellings in the larynx, but the disease is rare in this organ. **Urticaria** also occasionally affects the laryngeal mucous membrane, and the symptoms depend upon its extent. **Lichen ruber planus** is more usually observed in the mouth and fauces than in the larynx. **Impetigo herpetiformis**, **erythema nodosum**, and **erythema multiforme** are rarely observed in the larynx.

Involvement of the larynx occurs in all cases of **leprosy**, though it may be late in the disease. Following the symptoms of a simple catarrh, diffuse or circumscribed infiltrations occur, which mostly affect the epiglottis, changing its contour so that it may assume the shape of an omega, Ω . The infiltrations break down and various sized ulcers result. The tissues are destroyed, or white, glistening scars are formed, which

tend to the development of adhesions and stenosis. Although an anesthetic condition of the mucous membrane develops, there is a sensation of burning and tickling in the throat, which may even cause attacks of coughing. Dyspnea may become a prominent symptom.

PATHOLOGY.—Symptomatic laryngitis is ascribed to the penetration into the laryngeal tissue of micro-organisms, especially *Streptococcus pyogenes*, *Staphylococcus*, *Pneumococcus*, and *Bacillus coli communis*. The germs are thought to penetrate the deeper structures through minute abrasions of the surface or by way of the lymph-channels, the blood, etc. Neighboring inflammatory foci are especially prone to cause infectious disorders of the larynx.

TREATMENT.—The treatment of symptomatic laryngitis does not differ from that of acute laryngitis or edema of the larynx when the local manifestations are such as to warrant assimilation with these disorders. As a rule, the laryngeal manifestations of infectious diseases are slight, but the possibility of complications in this direction should always be borne in mind, owing to the rapidity with which they may prove fatal when untreated.

CHRONIC LARYNGITIS.

SYMPTOMS.—As a result of frequently repeated attacks of acute laryngitis, or of continued exposure of the larynx to conditions capable of maintaining a prolonged hyperemia of the larynx, a chronic catarrhal process is developed. Exacerbations of hoarseness, a sensation of rawness and heat, and the presence in the laryngeal cavity of secretions—mucoid or mucopurulent—giving rise to

a constant desire to "hem" constitute the main symptoms of this condition.

Chronic laryngitis is most frequently met with in singers. Hoarseness in these represents the most important symptom; it may be continuous or occur only after a few bars have been sung. This is usually accompanied by a feeling of local fatigue, heat, and constriction. The voice is usually lowered in pitch and may be veiled, muffled, or complete aphonia may exist. Pain is sometimes complained of. Cough provoked by sensation of itching or pricking frequently occurs as a prominent symptom. Slight hemorrhage and bloody expectoration are occasionally noted.

In some cases these symptoms present themselves upon the least exposure, disappearing after a few days. As the attacks are repeated, however, they become more resistant to therapeutic measures, and the local disorder becomes permanent symptomatically as well as pathologically. Hoarseness is then continuous. Warm weather, however, is apt to bring temporary relief.

The laryngoscopical appearances vary considerably, and are proportionate to the degree of active inflammation. The evidences of local hyperemia are nevertheless always present, and vary from a slight arborescent and light-pink tinge suggestive of congestion to a bright-red hue indicative of violent inflammation. The epiglottis is also congested, enlarged vessels coming over its posterior surface, while the arytenoepiglottic folds appear thickened, the tumefaction involving the entire larynx in marked cases. The surface is irregular and sometimes quite bosselated. The general red-

ness is not so marked as in some cases of acute laryngitis; it is apt to assume a brownish or violet coloration. The vocal bands are also more or less congested; the congestion may either be limited to a small portion of their surface or involve their entire area. Small masses of stringy, cream-like mucus are often to be seen, forming films, when the glottis is opened.

Sometimes the vocal bands appear relaxed and their thickened edges do not seem to come accurately together, an elliptical opening being occasionally observed between them. This want of parallelism is due to muscular inadequacy sometimes affecting but one side.

Shallow abrasions of the epithelial covering are occasionally met with, especially in the interarytenoid space. Deeper ulcerations, sometimes leading to perichondritis, have been observed by various clinicians.

The secretions are sometimes very copious, especially when, in the latter part of an active exacerbation of vocal disability, the patient tries to use his voice. This condition is termed *laryngorrhea* by some authors.

The terms *dry laryngitis* and *laryngeal osena* have been given to a condition occasionally met with in which the secretion, besides being mucopurulent, is prone to adhere firmly to the mucous surfaces and to become partly desiccated in this situation. The dry crusts formed, by impeding the free passage of air, give rise to more or less dyspnea, while the breath is rendered fetid. Laryngoscopically examined, the larynx appears red and dry, with greenish crusts closely adhering to parts adjoining the vocal cords either above or below.

ETIOLOGY.—In singers, officers, hucksters, etc., who are called upon to use the voice excessively, chronic laryngitis may occur as a primary affection, but in persons who do not use their vocal organs professionally, the primary cause can usually be traced to some disorder of the adjoining cavities, nasal, nasopharyngeal, and pharyngeal. A dusty or smoky atmosphere may induce chronic laryngitis, but the other portions of the upper respiratory tract are involved in the inflammatory process.

The rheumatic and gouty diathesis, gastric and hepatic disorders, the abuse of alcoholic beverages, and all the factors enumerated under the heading of ACUTE CATARRHAL LARYNGITIS may act as causative factors when exposure to them is prolonged.

Dry laryngitis has been ascribed to many affections. In some cases it is but a manifestation of a general atrophic process involving the mucous membrane of the upper respiratory tract and may thus be identified through the presence of Löwenberg's bacillus.

In the very few cases that I have met with, dry laryngitis, when not accounted for by a nasopharyngeal affection or syphilis, was found associated with a gouty diathesis. The infraglottic space seems to be the favored region for the formation of the greenish crusts observed in this condition.

Chronic inflammatory disorders of the larynx are more frequently observed in men than in women, doubtless because the former are more exposed to the etiological factors outlined than the latter. Smoking and drinking are prolific indirect causes, as stated, and these habits are most

generally indulged in by the male sex. Chronic laryngitis can occur at all ages.

PATHOLOGY.—Dilatation of the blood-vessels through paresis of the vasomotors, interstitial infiltration which may lead to hypertrophy and thickening, are the main pathological features attending a case of uncomplicated chronic laryngitis. The superficial vessels tend to become varicose, tortuous veins being observed, especially in regions—such as the ventricular bands, the interarytenoid membrane, etc.—where the tissues are lax. The glandular elements take an unusually active part in the inflammatory process of some cases, constituting what has been termed a *glandular laryngitis*. Rounded sessile projections, differing but slightly from the neighboring tissues in color, have been called *chorditis tuberosa* or *trachoma of the larynx*, but these are probably but mere localized hypertrophies, strictly associated with chronic laryngitis. *Chorditis nodosa* (singers' nodes) is a circumscribed hyperplasia of the epithelial and the subepithelial layers, and is situated on the edge of one or both cords, usually at the junction of the middle and anterior thirds. *Pachydermia laryngis* is usually noticed near the posterior end and on the margins of the cords as a rounded, oval or irregular, wart-shaped projection of a grayish or grayish-white color, with a corresponding depression on the other cord. The tissues beneath the vocal bands often take part in the inflammatory process, producing hyperplastic enlargement of the subglottic tissue, which is known as *chorditis hypertrophica inferior*, or *chronic subglottic laryngitis*. *Chorditis hypertrophica superior*, or *prolapsus ventriculi Morgagni*, is a hy-

peritrophic catarrhal condition of the ventricular folds, involving also the upper surface of the vocal cords and tending to the formation of pads and polypi, which project into the larynx.

TREATMENT.—The association so frequently noticed of chronic inflammation of the nasopharynx and of the larynx renders it imperative always to examine the entire upper respiratory tract when continued hoarseness is complained of. This is further supported by the fact that cases are often met with in which no benefit whatever is derived from treatment limited to the larynx until attention is given to the nasopharyngeal surfaces. **Cleanliness** of these parts, in fact, may be considered a *sine qua non* of success in 90 per cent. of cases. The same remarks may be applied in connection with concomitant disorders of other organs.

In many cases the laryngeal inflammatory process is sustained by disorders of the gastric, hepatic, and renal systems, all of which require close scrutiny.

Attacks of hoarseness in professional vocalists are often but exacerbations of chronic laryngitis, a deficiency of lubrication of the vocal bands being the main local factor. This condition may successfully be combated by the administration every two hours of 10 grains (0.65 Gm.) of **ammonium chloride** in a tumblerful of water, and the topical use of a **warm spray** of a saturated solution of **potassium chlorate** at the same intervals. The doses are so managed that the last one should be taken at least about three hours before a performance. This avoids exposure during the subsequent stage of perspiration. A lozenge containing 10 grains (0.65

Gm.) of **ammonium chloride** taken between the acts is of benefit in many instances.

In singers cocaine and the suprarenal preparations should not be applied in the larynx. They are goading spurs to a group of already tired nerves and muscles. Electricity and strychnine, except late in the treatment, are also contraindicated. It is on the simple astringents that the writer relies to check the catarrh and remove its effects, preferring **alum** and **zinc chloride**, the former in an atomized 2 or 3 per cent. solution, the latter in a 1 or 2 per cent. solution used as a spray or on an applicator, preferring the Burgess atomizer on account of its long, smooth tip and its finely divided spray. Grayson (Jour. Amer. Med. Assoc., Apr. 6, 1912).

In the treatment of diseases of the upper air passages in singers complete rest, with the use of **whispered-word method**, is indicated with inhalation of the following mixture:—

R. Tinctura benzoini

composita ʒj (30 c.c.).

Olei pini ʒxv (1 c.c.).

Mentholis ʒss (2 (gm.)).

Camphora gr. xv (1 Gm.).

Sig.: Add teaspoonful to 1 pint of warm water and inhale, t. i. d.

Singers do not stand severe measures well. The utmost gentleness should be used. Stivers (Calif. State Jour. of Med., Dec., 1912).

The characteristic congestion of this affection, and even the superficial erosions frequently encountered, will often yield to a **detergent spray** of **sodium bicarbonate**, **borate**, and **salicylate**, 3 grains (0.19 Gm.) of each to the ounce (30 c.c.) of water, applied copiously three times a day to the entire upper respiratory tract—the nose, the pharynx, and the larynx.

After cleansing, even the slight erosions should be touched with stronger agents. Solutions of **silver**

nitrate are most effective, but demand considerable dexterity if laryngeal spasm is to be avoided. The laryngeal forceps must be used, its tip, covered with a cotton pledget, being gently applied to the mucous membrane. **Resorcinol** is an effective agent in a solution containing 7 grains (0.45 Gm.) to the ounce (30 c.c.). A 20-grain (1.3 Gm.) solution of **iodoform** in **benzoinol** is a very effective remedy, but the difficulty of keeping the atomizer free when benzoinol is used renders its employment obnoxious to the patient. The infraglottic region should not be overlooked when local applications are made, the patient being directed to inhale deeply when the atomizer is being used.

Iodol might be substituted, but it possesses irritating properties when used in strong solutions; 5 grains (0.3 Gm.) to the ounce (30 c.c.) is the maximum strength that an inflamed larynx can stand with benefit. Solutions of **zinc sulphate**, **copper sulphate**, and **alum**, 5 grains (0.3 Gm.) to the ounce (30 c.c.), may be substituted should the other agents recommended not be obtainable.

Mild cases, especially those in which there exists involvement of the infraglottic tissues, are greatly benefited by **sodium benzoate**. Exacerbations are sometimes quickly stopped with 5-grain (0.3 Gm.) doses administered every three hours, in addition to the local measures recommended.

In certain cases the vocal bands will present, during an exacerbation of the catarrhal process, the greatest amount of congestion as compared with other parts of the laryngeal cavity. Their mucous membrane, as stated, appears thickened, bosselated, and very red at the edge, the voice

being coarse and screechy when an effort to sing is made. This form of chronic laryngitis is characterized by frequent exacerbations, and finally costs a singer his voice unless he stops singing for a while and undergoes active local treatment. Labus, of Milan, proposed flaying of the vocal bands in these cases, and obtained several satisfactory results. After thoroughly anesthetizing the larynx he tore off with a sharp square-tipped laryngeal forceps the superficial layer of membrane of the vocal bands—a procedure followed by slight hemorrhage, a few days' aphonia, and final recovery of the voice. Sajous has used for the same purpose fused **chromic acid** to destroy the thickened mucous layer, obtaining equally satisfactory results. **Cocaine** causing a copious flow of lubricating fluid from the lateral tissues when applied to the larynx for a certain length of time, it is necessary to use the acid as soon as possible after the application of the 25 per cent. solution.

The chromic acid, fused by heat to the end of a covered probe, such as MacCoy's, immediately before the anesthetic, is then applied to the surface of one of the vocal bands, while the patient, having been told to make a sound, brings both bands into apposition. This enables the operator to avoid cauterization of their edges—an important point in the preservation of the voice, especially in women. But little if any disturbance follows, and after a few days hardly a trace remains of the cauterization, except a spot presenting less redness than the surrounding parts. The applications should be made twice a week until all traces of localized congestion or bosselated areas have disappeared.

When laryngitis is aggravated by gastric, hepatic, or intestinal disorder, especially in drinkers and smokers, attention to these conditions should, of course, form an important part of the treatment. In patients who smoke considerably the congestion is often maintained simply by the irritating action of the air contaminated with smoke. Sitting in a smoking-car or in a room in which others are smoking is, therefore, as bad as if the patient himself were smoking.

In dry laryngitis attention to the nasopharyngeal disorder also forms an important part of the treatment. Detergent and disinfecting sprays are of great use, but must be employed for a considerable time. **Chlorate of potassium** in a saturated solution, and **potassium permanganate**, 3 grains (0.2 Gm.) to the ounce (30 c.c.), are effective agents, while **listerine** and water, equal parts, may also be recommended, to alternate with either. **Potassium iodide**, administered internally, 5 grains (0.3 Gm.) three times a day in half a glassful of water, tends to increase the laryngeal secretions, as it does those of the nasal cavities, especially in persons who are sensitive to its physiological effects. **Pachydermia laryngis** may be treated with **chromic** or **trichloroacetic acid**. When singers' nodes are large enough to cause discomfort, they may have to be **removed** with forceps. When a gouty or rheumatic diathesis can be traced, **colchicine** or **sodium salicylate** is indicated. (See GOUT and RHEUMATISM.)

TUBERCULOSIS OF THE LARYNX.

DEFINITION.—A tuberculous, primary or secondary, infiltration of the glandular elements and connective

tissue of the larynx characterized by tumefaction and ulceration and giving rise to dysphagia, aphonia, and dyspnea.

SYMPTOMS.—Tuberculosis of the larynx is often present in cases of pulmonary tuberculosis, and, were all the latter systematically examined laryngoscopically, lesions so situated as to preclude active subjective symptoms would be found in the majority of cases. Unless marked hoarseness, aphonia, or local pain be complained of, the larynx receives but little attention; were it otherwise, a greater degree of comfort could be afforded consumptives than they obtain when the pulmonary disorder is alone treated.

The larynx may become infected either through the lymphatics or directly through invasion of the laryngeal tissues proper by the bacillus of tuberculosis. Whether an erosion is necessary or not in the latter case is not established; it is believed, however, that such an erosion is necessary.

Slight hoarseness, short periods of aphonia,—a couple of seconds' duration at times,—a sensation of dryness, and local heat represent the early symptoms generally met with. If there is a pulmonary trouble, the symptoms of the latter, especially the cough, cause the laryngeal trouble to be attributed to it. After a period varying in length, the local pain is increased by deglutition, and sometimes radiates to the ears. The hoarseness is now apt to become aggravated or the voice may be completely lost.

The symptoms of early laryngeal tuberculosis are limited in number and not so valuable as the signs. The earliest is usually a mere weakening of the voice, which may appear long before hoarseness is noted.

C. L. Minor (*Jour. Amer. Med. Assoc.*, Nov. 19, 1910).

Hyperplasia of a mammillated or other typical aspect, commencing at or near the subglottic portion of the base of the vocal process and gradually marked by a furrow in the vocal angle, is the most distinctive of the initial changes. Casselberry (*Jour. Amer. Med. Assoc.*, Nov. 15, 1913).

In 8 of 10 cases of phthisis complicated by laryngitis, in which tubercle bacilli had been demonstrated in the sputum, the writer obtained a positive Wassermann reaction, the latter being then tested in a control series of 10 cases of pulmonary tuberculosis. An average of 10 per cent. had a positive Wassermann, as compared with the 80 per cent. in the laryngeal group. He concludes, therefore, that a syphilitic soil may act as a predisposing cause of laryngeal tuberculosis. Morton (*Tubercle*, Jan., 1921).

Cough is not severe, as a rule; but it is peculiar, being usually husky and lacking in resonance. The general health may continue to be good as far as active constitutional symptoms are concerned, until the distress during deglutition becomes such as to cause the patient to reduce the amount of food he takes to avoid the pain the act involves. Indeed, the dysphagia is such sometimes as to render the taking of any food a source of dread to the patient, and constitutes the most marked of all the symptoms. It is especially severe when the epiglottis is the seat of the tuberculous ulceration or when the pharynx is affected. In fatal cases it is apt to persist and to become steadily aggravated. The pulse, temperature, and other general symptoms are those of pulmonary phthisis, but emaciation progresses more rapidly than in the latter disease, the pain during the deglutition causing

the patient to abstain from food as much as possible.

Examination of the larynx during the early stages usually reveals a characteristic feature: a pale-yellowish tinge, which sometimes reaches to absolute pallor. In the majority of cases a typical sign also appears: a pyriform swelling, or "clubbing," of the arytenoids, which causes these prominences to resemble small cushions if they are both enlarged, which is not always the case. In some instances, however, the larynx may be as red as usual, and even appear congested. After a short time, grayish, superficial erosions may be detected, which, after a while, become deeper and sharp-edged, and are surrounded by a narrow, red areola. A thick, tenacious secretion usually collects over them, which can only be removed with difficulty. The morbid process then extends in various directions until almost any part of the larynx and neighboring tissue is involved in the general trouble. Various excrescences or tumors may appear, so situated, sometimes, as to compromise the laryngeal aperture. It will be seen, therefore, that the lesion may be in the form of an infiltration, an ulceration, or a tumor. Involvement of the larynx with miliary tubercles is questionable.

DIAGNOSIS.—The pallor of the mucous membrane, especially marked posteriorly; the club-shaped masses over the cartilages of Wrisberg and Santorini, and, in a large proportion of cases, the turban-like epiglottis give the larynx a characteristic appearance when the local process is at all active. The ulcers are more superficial than those of a syphilitic larynx, and appear grayish rather than yellow,

as in the latter disease. The syphilitic ulcer is "punched out," with perpendicular and crenated edges; the areola is dark in hue, and the ulcer is usually situated anteriorly, in contrast to tuberculosis, which occurs in the region of the arytenoid cartilages. The cancerous ulcer tends to be raised by underlying accumulation of morbid elements, and is totally devoid of the pallor peculiar to tuberculosis. The pain is usually most acute during deglutition in tuberculosis, during phonation in syphilis, and constant in cancer. Early paralysis has appeared as a comparatively frequent phenomenon, manifesting itself even before any laryngeal changes are evident. The injection of tuberculin may aid in the diagnosis.

PROGNOSIS.—Spontaneous cure of the slight tubercular ulcers occasionally occurs (14 cases out of 3000, Heryng), but the normal tendency of a tubercular process in the larynx is toward aggravation. When the epiglottis is affected the chances of recovery are very slight. These are improved materially, however, if the patient can be removed to a mild and warm climate and when the general health can, by suitable dietetic means, out-of-door life, and the judicious use of creosote, be favorably influenced.

After-histories of 833 tuberculous patients discharged from the sanitarium 3 to 7 years. Of those with no laryngeal tuberculosis about 16 per cent. in the first stage died; 38 per cent. in the second stage died; and slightly over 70 per cent. of those in the third stage died; or for all the cases the mortality was just under 40 per cent. Of those with tuberculous involvement of the larynx, 43 per cent. in the first stage died; 63 per cent. in the second stage; slightly over 78 per cent. in the third stage

died; and for all combined the mortality was 70 per cent. The prognosis was uninfluenced by laryngeal involvement in third stage cases, but it was $2\frac{1}{2}$ times less favorable in the first stage when the larynx was involved than when not. St. Clair Thomson (Lancet, Oct. 18, 1919).

TREATMENT.—The treatment of tuberculosis of the larynx should be local and general. The indications for the general measures will be thoroughly reviewed in the article on TUBERCULOSIS, PULMONARY, and are *invariably* applicable when the larynx is diseased, whether primarily or secondarily.

Thorough **cleansing** of the laryngeal surfaces is an important feature of the treatment. This can be done most satisfactorily with a lukewarm solution of **sodium borate** and **bicarbonate**, 10 grains (0.65 Gm.) of each to the ounce (30 c.c.) of water, using an atomizer, or the familiar **Dobell's solution**. Care should be taken to relieve the surfaces of all purulent discharges, and thus prepare them for remedial agents. If this cannot be done daily by the attending physician, some person in the immediate surroundings of the patient should be carefully instructed; but under such circumstances the cleansing process had better be resorted to night and morning.

As a local application **Elsberg's** saturated solution of **iodoform in ether** has stood the test of time; it must be applied with the laryngeal forceps, a cotton wad being used. For the patient's home use, a solution of **menthol**, 20 grains (1.3 Gm.) to the ounce (30 c.c.) of **benzoïnol**,—an excellent agent for the purpose,—will not only relieve the suffering, but greatly assist the curative process.

According to Dundas Grant, Yeo's continuous respirator will check cough in laryngeal tuberculosis. The preparation generally used is as follows:—

R *Creosote* 3iij (12).
Spirit of chloroform,
Oil of pinus sylvestris of each 3iss (6).
Oil of cinnamon,
Oil of citronella,
 of each ℥v (0.3).
Menthol gr. v-x (0.3-0.6).

McFall has derived the best results locally from a fresh 3 to 5 per cent. solution of **formalin**. The larynx is first cleansed with an alkaline solution, and then a cotton swab saturated with the formalin rubbed over the surface. The burning sensation following is not especially painful except in the most advanced cases, and may be prevented by applying **cocaine** beforehand. The throat feels clearer, and in many cases the cough is eased by this treatment.

The writer, utilizing the necrosing action and slow cauterization of neutral **quinine hydrochloride**, employed this drug in a typical case of vegetant tuberculous laryngitis, and obtained transformation of this lesion into an infiltrated ulceration of good aspect, much more apt to succumb to the successful action of the usual remedies. Ceneistro (*Annales des mal. de l'oreille, du lar., etc.*, Mar. 3, 1913).

Absolute silence and a combination of **orthoform**, **iodoform** and **compound stearate of zinc** recommended. Coakley (*Jour. Amer. Med. Assoc.*, Jan. 28, 1922).

Chaulmoogra oil, first recommended by Lukens, was used by the writers in 40 cases. They gave daily injections of a 20 per cent. solution of the oil in liquid petrolatum into the larynx with a laryngeal syringe. In cases of moderate severity the symptoms were usually controlled by the treatment. Addition of **Lake's pigment** proved advantageous in some cases; this consists of **lactic acid**, 50 Gm. (1½ ounces); **liquor formaldehydi**, 7 c.c. (100 minims); **phenol**, 10 Gm. (150 grains), and distilled water to make 100 c.c. (3½ ounces). Other measures

mentioned are the **cocaine-epinephrin spray**, **orthoform**, **superior laryngeal nerve blocking**, and **epiglottidectomy**. Alloway and Lebensohn (*Jour. Amer. Med. Assoc.*, Aug. 5, 1922).

More active measures are resorted to by specialists, and **lactic acid** may be said to hold a high position in this direction. A 50 per cent. solution, well rubbed into the ulcerated tissues after they have been thoroughly anesthetized with a 20 per cent. solution of **cocaine** every three days, is often productive of excellent results, but only in cases in which the local lesion is limited in extent.

The patient should be placed at complete rest, especially as regards the use of the voice; only occasional whispering should be permitted. A spray is advocated consisting of **phenol** and **potassium chlorate**, of each 10 Gm. (2½ drams); **glycerin**, 200 c.c. (6¾ ounces), and distilled water, 1000 c.c. If cough is violent or frequent, a general **sedative** is given to obtain absolute rest of the larynx. Pure air, rest and **overfeeding** will generally heal the ulcerations in a few months. In severe dysphagia, **surgical intervention** is indicated. For superficial ulcerations, if other measures fail, weekly applications of 50 per cent. **lactic acid** may be made. For deep infiltrations, vigorous, deep **cauterization** is required. Healing may be accelerated by daily **heliotherapy** for 5 to 30 minutes. In desperate cases, applications of **paramonochlorphenol**, insufflations of **anesthesia** and **morphine**, **injections of alcohol** or **cocaine** into the superior laryngeal nerve, and free subcutaneous injections of **morphine**, may be availed of. L. de Reynier (*Arch. internat. de laryng.*, etc., June, 1923).

The local application of **lactic acid** is greatly facilitated by the continued use of **orthoform** either in powder or, as advised by Kassel, in the form of an emulsion containing **orthoform**, 25 parts; olive oil, 100 parts. The

burning sensation lasts only about a quarter of an hour, and is then succeeded by anesthesia, which commonly lasts from twenty-four hours to three and a half days. The patient is able to eat all kinds of food, and the appetite is greatly increased. A distinct diminution in the amount of secretion in cases of ulceration is noted, but otherwise it does not appear to have any local therapeutic value. Patients do not dread the lactic acid treatment if orthoform emulsion is used regularly. In some cases, in order to control the cough, or at least reduce it to a minimum, it may be necessary to resort to sufficiently large doses of **codeine**. The use of **tuberculin** may be found beneficial in incipient cases.

Exposure of the larynx to sunlight (**heliotherapy**) and **X-ray** or **Finsen ray** exposures have been recommended.

Direct **sunlight** has given very encouraging results. The author's first patient has remained cured for over 6 years. He wore a broad black hat and black spectacles and sat facing the sun, projecting on the larynx the sunlight received on the mirror of the laryngoscope placed in the throat, supervising the reflection of the rays with a hand-glass. He kept this up at intervals during the day, for a total of $\frac{1}{2}$ hour at first and later 1 hour daily. In 6 weeks, improvement was marked, and after 7 months there was scarcely a trace of the disease. In another case 2-hour exposures a day were made with equally favorable outcome. Collet (*Lyon Méd.*, Mar. 10, 1912).

Thirteen cases in which the **solar laryngoscope** proved useful. The mirror reflecting the sun's rays onto the larynx is made of an aluminum and magnesium alloy which reflects 85 per cent. of the actinic rays while absorbing most of the heat rays. The patient can apply the treatment himself. The

exposure is only 30 seconds at first, gradually increased to 10 minutes. A. M. Foster (*Med. Rec.*, Sept. 18, 1920).

The writer states that if the **sunlight** treatment is carried out thoroughly for 6 months in the infiltrative and mild ulcerative cases complete arrest may occur. Pain is alleviated even in the hopeless cases. Voorsanger (*Amer. Rev. of Tub.*, May, 1922).

Cure of 12 incipient cases by **X-ray** treatment alone. In other cases it is useful as an adjunct to other measures, chiefly in the infiltrative and proliferative types. Rickmann (*Munch. med. Woch.*, Nov. 10, 1922).

Exposures of the entire body to the **Finsen light** for periods of 10 minutes to $2\frac{1}{2}$ hours every other day result in cure in about 50 per cent. of cases. Strandberg (*Lancet*, Dec. 8, 1923).

The **curette** may be used to advantage when too much tissue is not involved in the tuberculous process. It should be limited, however, to primary and incipient cases, and to cases in which the pulmonary lesions are very limited in area. Under such circumstances the chances of success are quite fair. Unfortunately the procedure requires a degree of dexterity which an experienced specialist alone can possess, even with the assistance of a 20 per cent. solution of cocaine, which facilitates the operation and renders it comparatively painless. Heryng's or Krause's curette may be used, the operation being watched in the laryngoscopic mirror. Cicatrization is usually complete in three or four weeks, and considerable relief is afforded if cure is not obtained. The application of 50 per cent. **lactic acid** to the curetted spot serves to increase the efficiency of the treatment.

Among the more severe surgical measures at the disposal of the physician, **enucleation** of the diseased area with sharp forceps may be advanta-

geous when the infiltration is limited to a location, such as the arytenoid prominences, which may readily be grasped. **Thyrotomy** enables the surgeon to reach all parts of the larynx from the outside and to curette thoroughly any diseased surface. This should not be resorted to, however, when the disease is far advanced.

According to Lockard, **amputation of the epiglottis** in laryngeal tuberculosis is called for in every case accompanied by severe dysphagia. Any lesion that resists treatment should be excised.

Among 76 patients treated with **artificial pneumothorax**, 12 had laryngeal tuberculosis of greater or less severity. The mild forms promptly healed without other measures. Under application of powders or **mentholated oil** and strict enforcement of the rule of **silence**, even the 4 severest cases healed completely. Zink (Münch. med. Woch., Sept. 2, 1913).

Over 1500 **resections** upon 575 cases of laryngeal tuberculosis yielded complete cure in about 50 per cent. of those with simple, circumscribed involvement; in 25 per cent. of cases of medium gravity, and in 13 per cent. of grave and rapidly progressing cases. Spontaneous cure may occur under proper conditions of **altitude** and **heliotherapy**, but improvement in the pulmonary condition cannot be shown to have any favorable effect on the laryngeal tuberculosis. Operative treatment should be undertaken only in cases without fever, in which the pulmonary condition is stationary. T. Rüedi (Brit. Med. Jour., June 21, 1919).

The **galvanocautery** has been increasingly advocated to encourage cicatrization in cases of dense infiltrations and in those where the ulcers show a tendency to sluggishness. According to St. Clair Thomson it is safer and more certain to help than any other local measure.

Laryngeal tuberculosis is always a complication of pulmonary tuberculosis, even though the latter may not be apparent to the patient. The **galvanocautery** is not used to destroy the entire tuberculous area, but rather to cause a local reaction, bringing fresh blood to the part and producing fibrosis. Swollen and edematous arytenoids, ulcerations on the dorsal side of the epiglottis, and edematous conditions of the epiglottis are greatly benefited by a few punctures of the cautery point. Infiltrations on the vocal cords or ventricular bands respond well when lightly touched, care being taken not to injure the delicate musculature. In very early lesions, characterized by simple hyperemia and not causing pain, **vocal rest** is the only treatment; it may result in arrest or cure of the condition. J. B. Greene (Amer. Rev. of Tuberc., Sept., 1924).

The writer obtained 25 per cent. of complete repair of the laryngeal tuberculous process in 477 cases treated. He credits the **sanatorium régime** and the prompt use of local measures, **laryngeal rest**, insured by **silence** or **whispering**, and the **galvanocautery**, with these results. Of the 119 cases in which complete healing took place, 69 were still alive from 2 to 10 years afterward, while 50 had died owing to the virulence of their pulmonary disease, even though the larynx had remained well and cicatrized. Sir St. Clair Thomson (Lancet, Nov. 8, 1924).

Tracheotomy is sometimes resorted to, to give complete rest to the larynx or when dyspnea becomes a source of suffering or threatens to become aggravated.

It may be wise to resort to **tracheotomy** if the patient proves unable to conform to the rule of strict silence. It is indicated also, as in any other form of laryngeal obstruction, if the patient cannot breathe freely. T. R. Rodger (Jour. of Laryng. and Otol., Oct., 1925).

An important feature of the treatment is to enable the patient to nour-

ish himself properly. Unfortunately the dysphagia is always the most marked symptom, and the sufferings of the patient are sometimes excruciating. One of the most satisfactory methods is to apply a 4 per cent. **cocaine** solution with the atomizer, about five minutes before each meal, to the larynx, thoroughly bathing all its surfaces, and to alternate this every week with **orthoform** powder. The patient does not, in this manner, become habituated to either drug, and the beneficial effects of each are preserved. Kyle found that the **juice of the pineapple**, applied by means of a spray or applicator, is frequently efficacious in relieving the distress to a certain extent.

To obtain anesthesia Hoffmann has used a simple device with which the patient is able to insufflate, himself, the anesthetic powder and thus anesthetize the region before eating. It consists of an open cup at the end of a bent tube. The powder is placed in the cup, the other end of the tube introduced into the throat, and the powder inhaled through the tube.

The **deep injection of alcohol** into the superior laryngeal nerve has many enthusiastic advocates.

Method for relief of pain by **injecting alcohol** into internal branch of superior laryngeal nerve described. Cleanse skin with alcohol. With left hand grasp larynx to steady it and hold it prominently under skin of side to be injected. Left index finger seeks the comparatively tender point where internal branch of superior laryngeal nerve penetrates thyrohyoid membrane, a point about halfway between upper border of thyroid cartilage and hyoid bone, and about 1 cm. in front of superior cornu of thyroid cartilage. Hold finger firmly in place while needle is inserted at center of nail perpendicularly to a depth of 1 to 1½ cm., causing, if nerve accurately located,

pain radiating to ear. Then inject drop by drop ½ to 2 c.c. (8 to 32 minims) of 75 per cent. alcohol (with or without 1 per cent. cocaine), previously warmed, until original pain ceases or 2 c.c. (32 minims) have been used. Repeat next day if necessary. Lewy (*Laryngoscope*, Jan., 1911).

Following method of **injection of 80 per cent. alcohol into the superior laryngeal nerve** recommended: The rim of the thyroid cartilage having been located with the thumb and forefinger in front of the greater cornu, the needle is inserted about 5 mm. below this rim and slowly passed in to the upper margin, being directed obliquely upward and backward. It is then pushed on 3 mm. further and the injection made with alternate slight retraction and advancement of the needle. The pain in the ear is often not felt until the injection is made. It is not essential for the needle directly to strike the nerve; the injection of alcohol in its vicinity suffices. In 8 out of 10 cases there was freedom from pain for 2 days to 3 weeks.

In most of these cases, however, the writer later carried out **section of the superior laryngeal nerve**. It is always well to resect, as well as to inject alcohol, on both sides, even if the symptoms are unilateral, as the chances of failure are thereby reduced. An incision is made on either side of the larynx 4 cm. from the midline, extending from the hyoid bone to the middle of the thyroid cartilage. The tissues are cut to the cartilage and the upper edge located along the posterior border of the thyrohyoid muscle. The tissues are then further separated with hooks and the nerve located beneath the vessels (previously made tense) about 3 mm. from the margin of the cartilage. Nerve section is indicated where the general condition is good. Where ulcerations outside of the distribution of the superior laryngeal nerve are present, the writer injects a 2 per cent. solution of **vuzin** with equal amounts of a 1 per cent. solution of **procaine**. Leichsenring (*Zeit. f. Hals-, Nasen- u. Ohrenhkl.*, Nov. 4, 1922).

Injection of alcohol into the superior laryngeal nerve used in 13 cases of advanced lung tuberculosis with tuberculosis of the larynx. Four patients who could swallow practically no food were completely relieved. In one, pain recurred after 22 days, and was dispelled by another injection. In 2 cases relief was still almost or quite complete after 35 and 45 days. All cases, while relieved of pain, had varying degrees of difficulty in "pushing the food down"; this motor disturbance passed off in 1 or 2 days. Swetlow (Amer. Rev. of Tuberc., Nov., 1925).

Much of the suffering may be avoided in the later stages if, as suggested by Wolfenden, the patient will **lie on his stomach** on a bed and suck up liquid food through a tube from a receptacle placed on the floor. The food thus tends to enter the esophagus through the pyriform sinuses on each side of the larynx, and to avoid contact with the latter. Occasionally, **pressing the larynx forward**, away from the pharynx, with the palms of the hands on the sides of the neck will assist materially in deglutition.

SYPHILIS OF THE LARYNX.

This condition develops in the regular course of the disease contracted by impure intercourse, or it may be the result of the use of an infected instrument in the throat, although it is doubtful if the primary sore has ever been observed in the larynx.

SYMPTOMS.—The symptoms found are usually those of either the secondary or tertiary stage. The erythema of the second period presents the signs of a simple catarrh, accompanied by more or less secretion, and produces a hoarse or raucous voice.

As the disease progresses, the small, round-celled infiltrations break down

and result in the formation of superficial, clear-cut ulcers, best known as *mucous patches*, which are especially located on the margin of the epiglottis, in the central and anterior portions of the vocal cords, and on the postlaryngeal wall. The subjective symptoms are insignificant and may manifest themselves only in disturbances of the voice, which may vary from a slight hoarseness to complete aphonia.

The tertiary stage of the disease shows more advanced infiltrations and deeper ulcerations, with pronounced edema. The ulceration is quite characteristic, exhibiting a sharply cut, deep, crater-like depression with indurated edges, and the floor of which is covered with a slimy secretion. Involvement of the cartilage by the ulceration produces a chondritis. As syphilitic cicatricial tissue shows a decided tendency to contract, pronounced disfigurement, stenosis, and distortion frequently result, and may produce irreparable functional disorders. Paralysis of the vocal cords is not infrequent, usually due either to the infiltration of the muscles or to the pressure of affected glands upon the recurrent laryngeal nerve.

DIAGNOSIS.—This is usually not difficult, but occasionally considerable care may have to be exercised in an effort to differentiate between syphilis and tuberculosis. The history and the examination, the less destructive process and the more pronounced subjective symptoms in the latter disease, the presence of spirochetæ in one and of tubercle bacilli in the other, and the Wassermann test, will tend to dissipate the confusion.

The task of differentiation becomes more difficult, however, if the two diseases coexist in the same patient.

TREATMENT.—This is usually constitutional, although local conditions may demand careful attention, especially if cartilaginous necrosis has taken place. The usual **antisyphilitic treatment** should be instituted. It may be found advantageous to alternate the administration of **arsphenamin** with that of **mercury**.

Syphilis of the larynx seldom endangers the life of the patient. While the disease usually responds to appropriate treatment and the patient in time is relieved of symptoms, in extreme cases the contractions of the cicatricial tissue may be so great as to necessitate the performance of **tracheotomy**.

ABSCESS OF THE LARYNX.

This is found in tuberculous perichondritis, has been observed to follow erysipelas, and may also be of traumatic origin. The infecting bacteria gain entrance beneath the perichondrium and cause the formation of pus, which produces a tumor-like mass.

SYMPTOMS.—The symptoms are fever, pain as the result of the retention, loss of voice, and symptoms of suffocation because of the encroaching of the abscess upon the glottis.

TREATMENT.—The part should be anesthetized with cotton dipped in a 10 per cent. solution of **cocaine** and applied with Sajous's laryngeal forceps. An **incision** should then be made into the abscess with a curved laryngeal lancet and the pus evacuated. In extreme cases **tracheotomy** may have to be resorted to to prevent suffocation.

STENOSIS OF THE LARYNX.

This often follows high tracheotomy, or may result from morbid processes in the larynx or trachea, although extralaryngeal causes may occasionally lead to it. Aspiration of foreign bodies, injuries, diseases of the laryngeal walls, granulation and scars, nervous disorders, and pathological processes in neighboring organs are other possible sources leading to obstruction of the larynx.

SYMPTOMS.—The chief symptom is dyspnea. Of course, the narrower the lumen, the greater the danger of suffocation. Other manifestations, as well as the prognosis, depend upon the location and the cause of the stenosis.

TREATMENT.—When the lesion is acute and develops rapidly, a **tracheotomy** will bring relief and may even furnish a permanent cure, but if some constitutional disease is the primary cause in a slowly developing stenosis the relief from a tracheotomy will be only palliative. **Catheterization** of the larynx after the method of Schrötter may be found advantageous. **Intubation** under direct vision (see preceding article) offers the best prospects of cure. The main point in the treatment consists in preventing suffocation and determining and removing the cause.

When a laryngeal stenosis was the result of hyperplastic changes, some form of dilatation proved to be the most logical method of overcoming it. Gradual, systematic **dilatation by intubation** offers very favorable prospects of success. The tube with a low retaining swell and a wide head seems to meet a want in the treatment of this form of stenosis. In children hypertrophic laryngitis is largely responsible for a chronic larynx-

geal stenosis. In this particular affection tracheotomy is more apt to induce connective tissue changes than to effect a final cure. Homer Dupuy (*N. Y. Med. Jour.*, Apr. 5, 1913).

After tracheotomy, the larynx no longer being partly closed during expiration as it is normally, intrapulmonary pressure is abnormally low during this period, causing insufficient oxygenation, increased respiratory rate, and a state of pulmonary and cardiac fatigue which influences the prognosis unfavorably. To obviate this, the writer adapts to the tracheotomy tube a valve which closes during expiration, forcing the air to pass out through the larynx. An almost normal type of respiration results, and bronchial secretions can be coughed up. If the laryngeal orifice is particularly narrow, excessive pressure may be caused by the valve, which is thereupon removed intermittently, and can be replaced by an adult patient when he wants to cough or talk. Such excessive pressure occurs mainly in cases where tracheotomy or intubation has already been performed, the laryngeal obstruction being then apt to become more rigid. G. Zorraquin (*Presse méd.*, Apr. 4, 1923).

CHONDRITIS AND PERICHONDRITIS OF THE LARYNX.

These two conditions are so closely allied in their course, symptoms, and treatment that it is unnecessary to consider them separately.

SYMPTOMS.—The **arytenoid cartilage** is the one most frequently affected, although the cricoid and thyroid may be involved separately or in conjunction with the arytenoid. The epiglottis appears to be the least affected. The objective symptoms produced will naturally depend upon the cartilage involved and the extent of the inflammation. Involvement of the arytenoid is more frequently on one side than bilateral. Edema in the

region of the arytenoid may be sufficient to extend along the aryepiglottic fold, or beyond the region of the vocal cord. Mobility of the cord is usually interfered with. If the cricoarytenoid joint is involved, ankylosis may result, with permanent alteration of the voice. When necrosis of the cartilage develops, the area may be visible and the discharge of pus detected, especially if gentle pressure is made on the outside.

The **cricoid cartilage** is not infrequently affected as the result of ulcers on the posterior laryngeal wall, especially in tuberculosis and typhoid fever. If the swelling involves the arytenoid region as well as the posterior wall, it is fair to assume that both the cricoid and arytenoid cartilages share in the inflammatory process. Pronounced swelling in the pharynx and pyriform sinus will indicate involvement of the external perichondrium of the cricoid, while disease of the anterior arch will produce a swelling in the anterior region of the neck which will be tender on palpation.

Involvement of the **thyroid cartilage** will show an external or an internal swelling, according to the location of the inflammation. The internal swelling is usually in the region of the anterior commissure.

The firm attachment of the perichondrium to the **epiglottis** makes difficult its separation by any pus formation. The cartilage, therefore, is more apt to be eroded and necrosed, especially by tuberculous and syphilitic ulceration.

Among the subjective symptoms, pain, hoarseness, and dyspnea may be present. A characteristic symptom may be noted in the radiation of the

pain to the ear on swallowing. This may be agonizing, especially if the arytenoid, cricoid, and epiglottis are simultaneously involved. External pressure over the affected area may sometimes produce considerable discomfort. The extent of the hoarseness will depend upon the amount of hindrance to the mobility of the cords. Dyspnea may be a pronounced symptom, owing to the extensive swelling of the laryngeal tissue. The rupture of an abscess into the larynx, the impaction of a necrosed piece of cartilage in the glottis, or the fixation of the vocal cords may produce alarming symptoms.

ETIOLOGY.—Syphilis and tuberculosis seem to be the most frequent causes of chondritis and perichondritis of the larynx, although many other infections have been held responsible. Actinomycosis, glanders, and various other contributory causes may also occasionally be noted. Some form of traumatism may very easily be the etiological factor. Only occasionally, viz., in pyemia, acute polyarthritis, etc., is a metastatic chondritis or perichondritis produced.

PATHOLOGY.—The infecting organism leads to a suppuration between the perichondrium and the cartilage. As the abscess develops, the perichondrium is separated from the underlying cartilage and bulges forward. The cartilage, being deprived of its blood supply, is prone to undergo necrosis. When the abscess ruptures, the necrotic cartilage can usually be detected projecting from the abscess cavity.

PROGNOSIS.—The many complications of a serious nature which may occur tend to make the prognosis a very serious one. Especially is this

true in tuberculosis and cancer, while a syphilitic lesion can offer very little more encouragement.

TREATMENT.—If possible, the cause should be determined and the treatment regulated accordingly. When the abscess develops, it should be evacuated, the **incision** being made with a guarded laryngeal knife. If the pointing is externally, as sometimes happens in the so-called external perichondritis, the evacuation of the pus should not be difficult. The respiration should be carefully watched and **tracheotomy** performed at the first evidence of excessive embarrassment. Resort to **narcotics** may be necessary to relieve the suffering. **Ice** internally and externally may give a certain degree of relief when the lesion is due to trauma.

In acute perichondritis, seen early, the treatment is brisk **catharsis**, **rest in bed**, **rest of voice**, and sometimes **local blood-letting**. If cough troublesome, inhalations of **compound tincture of benzoin**. When abscess seems inevitable, **hot fomentations**, with free **incision** under local anesthesia when it is localized. If there is much edema, a spray of **cocaine** and **adrenalin**. F. A. Will (Jour. Iowa State Med. Soc., Nov., 1922).

DISEASES OF THE LARYNGEAL JOINTS.

Inflammations of the joints of the larynx are probably more common than is usually realized, their apparent rarity resulting from the difficulty of properly interpreting the indefinite symptoms and from the lack of sufficient post-mortem investigation. Involvement of the laryngeal joints is not uncommon in cases of rheumatic or gonorrheal arthritis, while some of the infectious diseases, *e.g.*, typhoid fever, diphtheria, variola,

tuberculosis, and syphilis, may manifest symptoms indicative of extension to the parts. The cricoarytenoid joint is that usually affected. A serous or seropurulent exudate may appear; the periarticular tissue may or may not become infiltrated. The patient may be conscious of a feeling of tension during activity of the throat. The sensation may become aggravated on touching the sensitive spot with a probe or finger. A crackling noise produced by gentle pressure on the upper and back part of the thyroid cartilage is thought to be pathognomonic.

PARASITIC INVASION OF THE LARYNX.

Animal parasites seldom gain entrance to the larynx, although small insects may be inhaled during a strong inspiration. *Trichinæ* seem to show some preference for the laryngeal muscle in which to encapsulate, and *ascarides* have been known to crawl into the larynx.

Vegetable parasites are also found in the larynx, though very infrequently. *Thrush* has been observed to extend from the pharynx. The presence of *leptothrix* has been described.

From reported cases, *actinomyco-sis* has been found as a secondary lesion; Arrowsmith, however, has recorded an instance of actinomycosis in which there was apparently a primary laryngeal infection.

SCLEROMA OF THE LARYNX.

This is a rare disease in this country, but it is frequently encountered in certain parts of Europe. It is very seldom primary, but usually occurs as a continuation of the same disease in the nose and pharynx. The scleroma

bacillus is thought to be responsible. An inflammatory infiltration manifests itself below the vocal cords and presents a typical picture of hypertrophic subglottic laryngitis. Extension may occur along the trachea, and even into the bronchi, but more frequently the disease spreads to and involves the ventricular folds, the arytenoid cartilages, the aryepiglottic folds, and the epiglottis. The development of pad-shaped or even smaller nodular infiltrations of a pinkish or bright-red color and of hard consistency is noted.

SYMPTOMS.—These are usually of a catarrhal nature. The formation of scabs and crusts may give rise to the offensive odor characteristic of *ozena*. The diagnostic features of the disease are its coexistence within the nose, throat, and larynx, its exceedingly slow and painless progress, the peculiar odor of the scabs, the conspicuous pale infiltrations, and the absence of ulceration.

TREATMENT.—This is largely symptomatic. The condition may be influenced by the use of the **Röntgen rays** or of **radium**. Less conservative measures may become necessary if stenosis develops to any extent.

FOREIGN BODIES IN THE LARYNX.

The foreign bodies that may become engaged in the larynx may be said to represent almost anything that may be introduced into the mouth. A large mass of meat totally beyond the dimensions of the cavity may dip one of its extremities into the latter, and cause fatal dyspnea by acting as a stopper, or it may become jammed between the pharyngeal wall and the end of the epiglottis, and thus also

cause immediate asphyxia. Tooth-plates, among the larger objects, are also frequent intruders in this region. Those which most frequently become lodged there, however, are principally articles of diet,—bones, bread-crusts, fish-bones, etc.,—which are drawn into the air passages during a fit of laughter, just as the act of deglutition is being performed. Their penetration into the air tract depends greatly upon their size, small objects being frequently drawn into the trachea, while large objects remain in the upper part of the cavity.

SYMPTOMS.—Immediate and violent retching, or coughing if the passage is not entirely occluded, follows entrance into the larynx of any object: a reflex act calculated to dislodge it. Sometimes this succeeds, the foreign body is coughed up and out, and the patient recovers at once, although his throat may remain painful for several days. When the foreign body is large enough to fill the laryngeal cavity sufficiently to occlude it, and the first expulsive effort does not succeed, the patient, having comparatively emptied his lungs of air, finds it impossible to inhale; he makes desperate efforts to draw air into his lungs, each effort causing the offending object to impact itself more tightly in the glottis. In the great majority of cases, however, the object is of such a shape and form that sufficient air is permitted to enter the lungs to keep the patient alive. In this case the first paroxysm, although severe, subsides; violent paroxysms of coughing follow, and, after a few minutes, comparative comfort is enjoyed until another coughing spell brings on dyspnea and a renewal of the first symptoms. After a time,

the larynx seems to become accustomed to its new occupant, and a small object may even be forgotten and ejected in a fit of sneezing or coughing long after. In many cases, however, such is not the case, and organic lesions may be caused which may endanger the patient's life. The inflammation occasionally extends to the lungs, and a fatal result may be caused by pneumonia.

Again, notwithstanding the spontaneous expulsion of a foreign body, secondary inflammation may follow and endanger the patient by edema of the larynx. Under such circumstances, the patient at once experiences the preliminary stages of asphyxia; he gasps for breath and unless assistance be at once provided may die in a few moments. This is only apt to occur, however, when a mass totally occluding the larynx, such as a piece of dough or meat, becomes impacted.

Case in which a small piece of bone passed down the trachea and was lodged in the lower air passages, where it produced the symptoms of a diffuse catarrh. A year and a quarter later the foreign body was expectorated during a severe fit of coughing and then the general condition of the patient rapidly improved. Ritter (*Med. Klinik*, Aug. 27, 1911).

TREATMENT.—The simplest means are sometimes sufficient to dislodge an impacted body. A **slap on the back** during an expulsive effort while the patient is in the knee-chest position may succeed. At times, the object remains over the aperture and can easily be removed with the finger. The epiglottis may be held down by the impacted body so as to completely close the laryngeal aperture;

the finger can also be used in this case.

When the foreign body presents a certain degree of weight, such as a piece of coin, a bullet, etc., an effort may be made to cause its fall from the larynx by **inverting the body**, the patient standing on his hands while his feet are held up; or, he may be placed face downward, on a table, one end of which is then raised as high as possible.

Pins and needles, tacks, and bones—*i.e.*, objects having a tendency to penetrate into the tissues when efforts at expulsion are made which cause them to increase their hold—can be withdrawn by means of **forceps** with the assistance of the laryngeal mirror. With the aid of **cocaine**, the operation is greatly simplified; a 10 per cent. solution should be applied to the laryngeal membrane and all the parts around the larynx, including the epiglottis and the base of the tongue, and will so anesthetize the throat as to render the extraction of the foreign body a comparatively easy task. Any laryngeal forceps may be employed to grasp small objects, while Fauvel's, Mackenzie's, or Cusco's may be used for large ones.

Of far greater value is **bronchoscopy**. The Jackson and the Brüning instruments for direct inspection of the lower air passages have supplanted almost entirely the earlier methods of indirect examination. Either with the speculum or the proper-sized tube, if the foreign body is below the vocal cords, the intruder can usually be located and removed with greater ease and less distress to the patient than by the indirect method formerly used. (See the preceding article: **LARYNGOSCOPY**, etc.)

Eleven cases are recorded in which **electromagnets** were used for the extraction of metallic bodies from the trachea and bronchi. Seven of these cases were successful. The magnet may also attract the foreign body and thereby shorten the search when an external operation becomes necessary. In the vast majority of instances, however, the bronchoscope remains the instrument of choice. Samuel Iglauer (*Laryngoscope*, Jan., 1914).

Case of a man of 40, complaining of aphonia and great difficulty in swallowing, but none in respiration. Two days before, a piece of lobster claw had apparently stuck in his throat, causing an attack of suffocation. Laryngoscopy showed such edema of the arytenoids as to conceal the vocal cords. Upon cocaine-adrenalin anesthesia, the ring-like end of the lobster claw was seen in the glottis, and the patient was found to be breathing through the claw, which was lodged in the larynx like an intubation tube. It was removed with some difficulty and was found to be 38 mm. long, 8 mm. in diameter at one end, and 5 mm. at the other. In a few days recovery was complete. H. Philippides (*Rev. de laryng.*, etc., June 15, 1923).

Eighty-five cases of lodgment in the larynx of the fruit of the sand spur or sand bur (*Cenchrus tribuloides*) are on record. The weed occurs from Maine to Florida and Colorado, and in the far South is very common near the coast. The bur bears 30 to 40 spines, each with many sharp, curved barbs which readily break off at their tips, and which, when young, contain irritating formates. Ten children with a sand bur in the larynx for over 24 hours presented a clinical picture resembling laryngeal diphtheria, with prostration, temperature 100° to 102° F., pulse 100 to 140, mild cervical adenitis, marked hoarseness, increasing dyspnea, sometimes cyanosis, and locally a grayish, elevated exudate, often obscuring the foreign body, with inflamed and sometimes edematous surrounding area. Hoarseness persisted for weeks after removal of the bur, on account of the

broken off barbs. H. M. Taylor (Ann. of Otol., Rhinol. and Laryng., June, 1924).

If the necessary instruments are not at hand, either for direct examination or tracheotomy, and suffocation is threatening, the **trachea** may be opened with a **penknife** and the wound kept patulous with carefully cleansed **hairpins** the curved ends of which are bent into hooks. The sharp ends being also bent into hooks in the opposite direction, thus forming an S, the pins are secured by means of a piece of tape passed around the patient's neck. Or, the **thyro-cricoid membrane** may be **divided**, thus furnishing a sufficient opening for the admission of air until more decided measures can be adopted. Before doing this, however, it is advisable to ascertain as nearly as possible the location of the foreign body, to avoid making an unnecessary opening in case it should have fallen into the trachea. The **location** of the **foreign body** may often be ascertained by **auscultation**, a whistling noise being audible at the point of impaction; a stethoscope may be used for the neck; in the great majority of cases, however, the **Röntgen** rays will have to be employed.

Analysis of 612 cases of foreign bodies showed carelessness in this order of frequency: (a) In putting inedible substances in the mouth; (b) in preparation of food; (c) in eating and drinking; (d) in permitting children to play while eating, and (e) in permitting toothless infants to eat things needing mastication. Of 590 cases, 492 were in children under 15 years. Chevalier Jackson (Trans. Sect. on Laryn., Otol. and Rhinol. of Amer. Med. Assoc., 99, 36-56, 1917).

Tracheotomy is occasionally performed to enable a foreign body im-

pacted in the trachea to be coughed out. The opening made in the wind-pipe should be longer than for the introduction of the cannula: $1\frac{1}{4}$ inches for an adult and about 1 inch for a child. The spontaneous extrusion of the foreign body is thus greatly facilitated. This method, however, is now seldom used since the introduction of the Jackson and the Brünings instruments.

Low tracheotomy, for some time obsolete, has been revived by Killian for the introduction of the examining tube and the removal of the foreign body from the bronchi, when it is impossible, for any reason, to insert the instrument through the mouth.

Jackson frequently removes foreign bodies from the lower air passages without either local or general anesthesia, but few are so skillful as to obtain the desired result without first thoroughly anesthetizing the mucous membrane with cocaine or administering a general anesthetic.

LARYNX, NEUROSES OF.

LARYNGISMUS STRIDULUS, OR SPASMODIC LARYNGITIS.

This is an affection of poorly nourished or weak children in which dyspnea, caused by spasmodic closure of the laryngeal aperture, suddenly occurs.

SYMPTOMS.—The attacks usually come on at night while the child is asleep. Awaking suddenly, the patient gasps for breath and shows every evidence of prompt suffocation without cough or hoarseness. The pulse becomes weak, cold sweats and cyanosis soon come on, and in a few moments the child may be at death's door. Often, however, after a few gasps, a quantity of air is suddenly

drawn into the lungs with a "crowing" sound, the respiration becomes more normal, and in a few minutes the child seems out of danger. This improvement is sometimes ephemeral, however, and the attack may return after a few minutes or hours, and continue several succeeding days and nights. The number of deaths in a series of 164 cases collected by Loos amounted to 14.

ETIOLOGY.—There being no inflammation of the larynx, the term "laryngitis" is not applicable, a spasmodic element alone prevailing, which is related to spasmophilia. It occurs about equally in children of both sexes, and may be initiated by a nervous shock or excitement such as occurs when children are severely punished or even scolded. It occurs mainly in children who have soft bones and cartilages, flabby muscles, and general weakness; hence rachitis has been considered a pathogenic factor in very many cases. The pressure of enlarged bronchial glands upon the vagus, adenoid vegetations, and hypertrophied tonsils seem to bear a close association with the disease. Gastrointestinal disorders and exposure to cold and damp are also common attendants of this disorder.

TREATMENT.—Measures calculated to meet the danger of suffocation, leaving the determination of its true nature until all immediate danger has been eliminated, are first indicated. A **warm mustard foot-bath** or a **general bath** usually serves its purpose very rapidly; sometimes **cloths wrung out of cold water** placed over the thyroid are sufficient, or the application of **hot water to the nape of the neck** may bring the desired relief. **Seizing the tongue firmly between the**

thumb and forefinger and making traction every two or three seconds will tend to excite the respiratory center by reflex action through the phrenic nerve. Should the jaws be set, the same result may be obtained by **deep pressure with the fingers on the tissue at the angle of the jaw**. Of value is the production of **emesis**, either by titillating the back of the mouth with a feather or administering **ippecac**. The triturate tablets of the latter drug have been particularly recommended, 4 or 5 of the $\frac{1}{100}$ -grain (0.00065 Gm.) tablets being given every ten to thirty minutes until emesis is produced. A few whiffs of **chloroform** or **ether** sometimes act favorably at once. The possibility of impaction of the epiglottis is to be remembered as a causative element, and, even should it be found free, no harm will have followed the **introduction of the finger**, which, in case of impaction, will raise it without difficulty.

The application of a **sinapism** over the **liver** tends to prevent recurrence of the attacks. The **bromides, chloral, opium, belladonna**, etc., also act advantageously. Exposures to the **ultra-violet rays** are strongly advised in the treatment of a constitutional spasmophilic tendency, when present.

Morphine injections sometimes cut the attack short in a few moments. When all means fail to re-establish normal respiration and the dyspnea continues marked, **intubation** should be practised. If instruments be not at hand to perform the operation, the **trachea must be opened** or a **catheter introduced into the larynx** to temporize until intubation instruments can be obtained.

There are 2 types of laryngeal spasm, 1 due to spasmophilia and the other

to enlarged thymus. Chvostek's sign distinguishes these 2, appearing only in the former. It does not occur, however, in infants below 6 months of age. There is a very frequent coincidence with congenital syphilis and with rickets. In the spasmophilic type the **ultra-violet rays** are curative. Exposures beginning with 1 minute and increased by the 5th day to 5 minutes are given, followed by a return to 1 minute. The total number is 20 to 30 daily exposures. Improvement is seen after 5 exposures, and after 20 Chvostek's sign and hypocalcemia disappear. In the type associated with enlarged thymus, **X-ray** treatment may be indicated. In both types **antisiphilitic treatment** should be given. G. Mouriquand (Médecine, Aug., 1925).

MOTOR LARYNGEAL NEUROSES.

The main varieties of **adductor paralysis**—*i.e.*, paralysis of the muscles which close the glottis—are: paralysis of the adductors or lateral cricoarytenoids; paralysis of the internal tensors of the vocal cords or internal thyroarytenoid muscles, and paralysis of the interarytenoid muscle.

PARALYSIS OF THE LATERAL CRICOARYTENOID MUSCLES.—

This variety of paralysis is that generally termed **hysterical aphonia**, owing to its prevalence among the female sex and the association it so often presents with disorders peculiar to them, neurotic and uterine. It usually comes on suddenly, the aphonia being generally total, including even, sometimes, the power to whisper. Some cases are able to sing, however, and the voice may also appear during laughter, sneezing, coughing, etc.; indeed, in every act involving vocal resonance, except talking. The vocal cords upon laryngoscopic examination are wide apart and fail to ap-

proximate when the patient is told to sound her voice, the formation of sound-waves being impossible. The mucosa in true cases of hysterical aphonia is pale. It is usually due to a shock or fright; sometimes no external cause can be found. There is, as a rule, a history of previous attacks.

TREATMENT.—In true hysterical aphonia the voice may return as suddenly as it disappeared without treatment. But therapeutic measures are required in the majority of cases, since prolonged paresis of the muscles is liable to promote their atrophy. The cases should be carefully examined and any abnormal condition corrected. **Strychnine** is always indicated. The voice can usually be brought back, by local applications of **electricity**, one pole, using Mackenzie's electrode, being inserted behind the larynx and the other, the negative pole, externally over the thyroid cartilage. A weak current is sufficient—indeed, at times, no current at all—to cure a case, the psychical effect being the main factor.

Citelli pushes the thyroid cartilage to one side with sufficient vigor to cause pain, taking the patient unaware. Almost invariably this **thyroid deflection** will lead to an immediate verbal protest.

The writer observed 6 cases of aphonia which began in the trenches. In 4 the voice returned on asking the patient to **phonate** with the laryngeal mirror *in situ* for the purpose of examination and a mild application of the **faradic current** was effective in the other two cases. J. F. O'Malley (Proceed. Royal Soc. of Med.; Med. Rec., Nov. 13, 1915).

PARALYSIS OF THE INTERNAL THYROARYTENOID MUSCLES.—This form of laryngeal paralysis is usually manifested by hoarseness or low-pitched huskiness.

The paralyzed muscles being tensors of the vocal cords, their mobility, as far as adduction and abduction are concerned, is practically unimpaired. When, therefore, the patient is asked to phonate while the laryngoscopic mirror is in position, the cords usually come together in the normal way, but, tension failing to simultaneously occur, an elliptical space remains between the margins of the cords. The coarse vibrations induced give rise to the characteristic voice. Paralysis of the internal thyroarytenoids may accompany various neuroses, especially neurasthenia. Local disorders, of a congestive kind, or excessive use of the voice are comparatively frequent causes of this variety of paralysis, which is, however, usually associated with other local motor lesions.

TREATMENT.—Total rest of the voice, faradization, increasing doses of strychnine, and massage of the anterior cervical region represent the indications for these cases, which, as a rule, readily yield to appropriate treatment.

PARALYSIS OF THE INTER-ARYTENOID MUSCLE.—This muscle is seldom paralyzed alone. Its position from side to side in the posterior wall of the larynx enables it to cause approximation of the neighboring portion of the cords about one-fourth of their length. When, therefore, it is paralyzed, only the anterior three-fourths of the cords are adducted, the posterior fourth remaining abducted and open. In the mirror a triangular gap may be discerned. As a result, vocal resonance is almost entirely prevented and aphonia is usually complete, or a peculiar, whistling tone is given to whatever voice may remain. It is usually caused by

prolonged catarrhal inflammation involving the interarytenoid space, and hysteria.

TREATMENT.—The treatment does not differ from that of other forms of paralysis. Any catarrhal condition that may be present should, of course, receive careful attention.

ABDUCTOR PARALYSIS.

Unilateral Paralysis of the Posterior Cricoarytenoid Muscles.—The vocal cords being separated or abducted by the cricoarytenoid muscles, paralysis of one of the latter causes the corresponding cord to remain adducted,—i.e., in the middle line or slightly beyond,—while the other cord acts normally, during phonation. The irregular, triangular space forming the glottic aperture is sufficient for normal breathing, however, in the majority of cases; dyspnea, therefore, is infrequently complained of, except under great exertion. The voice is seldom impaired, the only alteration being a certain degree of coarseness, especially marked after continued use of the voice. Examined laryngoscopically, the cord on the affected side will be seen to remain in the fixed position mentioned during inspiration.

Bilateral Paralysis of the Posterior Cricoarytenoid Muscles.—When both muscles are paralyzed, the cause is usually some central lesion. One has then a dangerous form to contend with, inspiration being almost prevented by the permanently adducted cords. The dyspnea is especially marked during inspiration; the cords being pressed downward and closer together by the air-pressure above them, through the suction induced below by the expansion of the chest. A whistling sound is heard, as the air

rushes through the small aperture left open through relaxation of the arytenoids. During expiration, the air forced up the trachea separates the cords, owing to the inclined plane of the infraglottic tissues. Though the voice is practically normal, the continuous dyspnea to which these patients are subjected is very distressing, and their continuous efforts to inhale after a few words have been uttered and the whistling noise produced give the condition a character which is not soon forgotten. Slight congestion of the tissues sometimes so increases the likelihood of asphyxia that **intubation** or **tracheotomy** is at once necessary.

ETIOLOGY AND PATHOLOGY.

—Paralysis of the abductors is frequently produced by pressure upon one or both vagi or their recurrent branches by various growths of the neck and thorax, goiter, esophageal cancer, etc. The left recurrent—curving, as it does, around the aorta—is particularly exposed to the pressure of aneurisms in this situation, causing unilateral paralysis. The motor nerves of the vagus being all derived from the spinal accessory, any growth of the brain involving the origin of the latter or the vagus itself may also give rise to abductor paralysis. Bulbar lesions, amyotrophic lateral sclerosis, and locomotor ataxia may be mentioned as among the neuroses most frequently complicated in this manner, while typhoid fever, syphilis, lead poisoning, etc., may also give rise to abductor paralysis through involvement of the nervous supply in the general toxemia. Again, the situation of the posterior cricoarytenoids outside and behind the larynx proper causes them to be

greatly exposed not only to involvement in neighboring inflammatory processes, but also to the mechanical effects of foreign bodies, hot liquids, or corrosives that may be swallowed. A long-standing paralysis of the posterior cricoarytenoid muscles is very significant of locomotor ataxia. The resulting stenosis is of slow development and the patient gradually becomes accustomed to the reduced air supply, so that, at first, he becomes dyspneic only during bodily efforts.

The writer being called to a case of dyspnea, found a marked abductor paralysis. He was obliged to do an immediate tracheotomy, but in the trachea he also found constriction. In spite of a long tracheotomy tube, the child died of exhaustion, and was found to have a large tuberculous lymph node pressing on the trachea. Delavan (Trans. Amer. Laryn. Assoc.; N. Y. Med. Jour., Feb. 2, 1918).

TREATMENT.—The likelihood of cure corresponds with the degree of amenability to treatment of the original cause. Whether it be syphilis, tuberculosis, aneurism, a cerebral neoplasm, etc., local treatment is absolutely subservient to that of the primary affection, and the treatment of the latter is therefore the first indication.

Measures must be adopted to stimulate the laryngeal muscles to action. **Faradization** is the most effective agent at our disposal. The laryngeal electrode (Morell Mackenzie's) is used as follows: The electrode being connected with the negative pole of a faradic battery, its extremity is introduced into the larynx, while the positive pole is connected with an ordinary surface electrode which the patient presses over the larynx externally, or with a necklet electrode.

The extremities of both electrodes should be covered with sponge or kid, to prevent stinging. To insure penetration of the current the electrode tip should be thoroughly wetted before each operation. The manipulation of Mackenzie's electrode is like that of an ordinary laryngeal forceps, the mirror being employed to note and conduct the localization of the tip of the instrument. The nearer the paralyzed muscle the application, the better. The electrode being in position, the finger-rest on the top of the handle is depressed, and firm pressure is exerted on the neck by the other electrode. At first this manipulation is quite difficult to perform, gagging and retching preventing the introduction of the instrument. After a few trials, however, the parts become more tolerant, and the application can be borne, in the majority of cases, without trouble. Cocaine anesthesia may be used in difficult cases, at least the first few times. Each application of the current should last but a few seconds, and be repeated several times at short intervals. One sitting every day should be obtained if possible.

The current may also be applied by placing one pole on each side of the neck externally. This method is very inferior to that just described. Better than it is **electrical massage**, which is carried out by placing the positive pole, thoroughly wetted, on one side of the larynx, and the fingers of the opposite hand (that holding the negative pole and in contact with the sponge) on the other side. The fingers, having become the conductors, are moved up and down, pulp down, and pressed into the surface of the neck, in the manner practised by masseurs. They must also be

kept wet by occasional immersion in water.

Strychnine, nux vomica, and other nerve tonics should be used. Strychnine is especially valuable, either by the mouth or hypodermically, beginning with $\frac{1}{60}$ grain (0.001 Gm.) 3 times a day, and gradually increasing to $\frac{1}{20}$ grain (0.003 Gm.).

Following **operation** to correct a median position of both vocal cords advocated: The arytenoid articulation and the muscles surrounding it are exposed by a curved incision. The arytenoid and lateral cricoarytenoid muscles are then cut, thereby relieving the fixation of the cartilages due to the shortening of the muscles. The arytenoid cartilages are brought into proper position by tampons of sponge rubber into which a suitably notched celluloid plate has been sutured. A. Réthi (Zeit. f. Hals-, Nasen- u. Ohrenh., Nov. 1, 1922).

DISORDERS OF SENSIBILITY.

Anesthesia.—Among the central causes of anesthesia of the larynx are hysteria, locomotor ataxia, bulbar paralysis, and other cerebral focal diseases. Diphtheria is the main peripheral cause. It often paralyzes the motor (inferior laryngeal) as well as the sensory (superior laryngeal) nerves, and is frequently associated with anesthesia and paralysis of the soft palate. Artificial anesthesia is produced by certain drugs, *e.g.*, cocaine, alpin, menthol, etc.

Hyperesthesia.—Various conditions may produce a hypersensitiveness of the larynx. Previous catarrhs, especially in smokers and drinkers, may be a predisposing factor. Tuberculous and anemic persons show a tendency to sensitiveness of the larynx. The condition is not infrequently noted in hysteria and neurasthenia. It is now a well-known fact

that certain abnormalities within the nose may affect the larynx by reflex action.

Paresthesia may be of central origin, or due to some local condition. It is usually found in patients suffering from hysteria or neurasthenia. Foreign bodies, which may or may not have been removed, are sometimes a contributing factor.

TREATMENT.—If possible, the etiological factor should be determined and corrected. The general health of the patient should receive careful attention. The **galvanic** or **faradic current** may be used to advantage in cases of anesthesia.

LARYNGEAL APOPLEXY (laryngeal vertigo, or laryngeal syncope) appears to be a neurosis affecting the co-ordination of the respiratory centers and the nerves of the larynx. The symptoms manifested clinically resemble an attack of apoplexy. A transient irritation and a burning sensation occur in the lower part of the throat, and cough follows, with dimness of vision, dizziness, and unconsciousness. The attacks are usually of short duration.

TUMORS OF THE LARYNX.

SYMPTOMS.—The location of a laryngeal tumor, its size, and its nature bear considerable influence upon the symptomatology. A growth situated anteriorly in the anterior commissure may, though small, so prevent approximation of the cords as to cause complete loss of voice; on the other hand, a large, soft growth located below the cords may not interfere with adduction and only give rise to the symptoms of chronic laryngitis. Paroxysmal hoarseness is often observed in such cases, especially

after loud talking or laughing. A small tumor situated above the cords may also give rise to very little trouble and cause no subjective symptoms. In the great majority of cases, however, persistent hoarseness is the first manifestation. Dyspnea follows and gradually increases until orthopnea is threatened. If at this stage the nature of the trouble be not recognized and the growth extirpated, the patient dies asphyxiated. Small growths with long pedicles are apt to titillate the laryngeal mucous membrane, and give rise to cough or spasmodic retching. A rattling noise or coarse gurgling is also sometimes heard when such growths are present.

Laryngeal tumors may be benign or malignant.

BENIGN TUMORS.

Benign tumors usually grow slowly, and dyspnea only comes on late in their history, unless an acute cold or any local inflammation causes temporary infiltration of the tissues, when dangerous symptoms may suddenly supervene.

Singers' Nodes.—These small growths, usually observed on the superior surface of the cords, or near their edge, and usually in the anterior thirds, are the result of overuse of the voice. The first manifestation is fatigue unusually soon after beginning to sing; this is followed by gradually increasing hoarseness. The tumor varies from a pin's head to a small split pea in size, and forms the center of an areola. Often the same spot in the opposite cord is also the seat of a growth. There are often several on both cords.

Papilloma.—This variety of growth is commonly met with, especially

in children, and represents over one-half of all laryngeal tumors encountered in practice. It is usually a multiple growth and varies much in size, shape, and position. The seat of predilection is usually the vocal cord, but it may be found in any other part of the larynx. It is ascribed to inflammatory disorders of the organ, especially when in subjects suffering from diathetic disorders, or showing familial traces of syphilis or tuberculosis. They are often attached to the anterior portion of the cord, near the commissure, and may be sessile or pedunculated. The numerous papillæ cause their surface sometimes to resemble that of a raspberry, especially when dark red in color. They may be yellowish, white, or pinkish. They are occasionally observed at birth, the infant being aphonic and showing evidence of dyspnea. Digital examination or bronchoscopy are necessary to recognize them in small children. While these growths are only benign in young subjects, they nevertheless show a marked tendency to recur. When they occur after middle life they should be looked upon with suspicion. Tuberculous growths of the larynx may be taken for papillomata.

Fibroma.—Fibromata may be assimilated to nasal polypus, though they are more opaque and resistant to pressure. They are smooth and usually sessile or pear-shaped, may be whitish gray or reddish, the latter color being due to sanguineous extravasation, through coughing, hemming, etc. They are generally found near the anterior commissure upon the cords, below them, or upon the ventricular bands. They sometimes become sufficiently large to com-

pletely fill the larynx and cause asphyxia. Overuse of the voice is also thought to be their main cause; they are usually found in men.

The other varieties of benign growths occasionally met with in the larynx are **cysts**, **angioma**, **chondroma**, **adenoma**, **lipoma**, **myxoma**, and **amyloid** and **thyroid tumors**. Pachydermia laryngis is sometimes considered a tumor.

TREATMENT.—In singers' nodes **rest** is the first requisite, talking especially being as much as possible avoided. The local use of astringent solutions is generally useless. The local application of **chromic acid** with a suitable instrument and by an expert, or **galvanocauterizations**, or, again, the use for sufficiently large growths of the **laryngeal forceps**, alone affords satisfactory results.

In the surgical treatment of singers' nodes the writer considers removal by **galvanocautery** preferable to ablation by forceps or curette. The amount of tissue removed can be more exactly gauged, and the sealing of the vessels and lymphatics by the heat generated does much to prevent postoperative infection. C. J. Koenig (*Annales des mal. de l'oreille*, etc., Nov., 1910).

While the so-called "singers' nodule" (chorditis nodosa) usually occurs in singers and public speakers, it may occur in anyone who habitually misuses the voice. While faulty breathing is a factor, the principal causes are the overtension of the extrinsic and intrinsic muscles of the larynx. After the patient has learned to use the voice properly, the cause is removed and the nodule will not reappear. F. B. Laurent (*Jour. Amer. Med. Assoc.*, Sept. 30, 1911).

In the cases of all other benign growths **removal** is also necessary. In small, sessile growths this may

sometimes be accomplished by **chromic acid** or **galvanocautery**. As soon, however, as a neoplasm reaches beyond the dimensions of a split pea, removal with **forceps**, Fauvel's or Mackenzie's, or better with the Jackson or Brünings instruments, should be resorted to, after anesthetizing the larynx with a 20 per cent. solution of **cocaine**. **Tracheotomy** sometimes becomes suddenly necessary when the growths are large. General anesthesia under such circumstances can rarely be used, lest the saturation of the pulmonary residual air with the anesthetic cause death. Benign tumors do not recur at the same spot, if they recur at all.

Three cases in which diffuse recurrent papillomas of the larynx, after operation, underwent retrogression under treatment of 5 Gm. (75 grains) daily for two weeks, then 0.5 Gm. (7½ grains) of **calcined magnesia** daily for a prolonged period. In veterinary medicine papillomas are very frequent, especially in the mouths of dogs, and the heroic, while empiric remedy is calcined magnesia. Claoué (*Annales des mal. de l'oreille*, etc., No. 1, 1911).

Case of papilloma of vocal cords cured by **radium**. The patient had had her larynx cleared out every six months for over 47 years by means of cutting punches. A second case, in a girl of 17 years who had an unusually sweet singing voice, became hoarse on account of the proliferation of these papillomata, which covered the whole of 1 vocal cord and ⅔ of the other. The writer did a tracheotomy under ether anesthesia, and through this wound passed a wire up through the larynx into the mouth. He thus drew up into the larynx a small smooth capsule containing 100 mg. of pure radium, between the vocal cords, where it was held for thirty minutes. Three months after this 1 treatment no

trace of the growth remained, the cords being entirely healthy in appearance and presenting no sign of disease or scar. Abbe (*Med. Rec.*, Apr. 13, 1912).

On the basis of personal experience in 5 cases, the writer concludes benefit or complete cure may be confidently expected from the use of **X-rays** in simple papillomatous vegetations of the larynx. A. G. Gray (*Va. Med. Mthly.*, May, 1919).

The writer obtained good results in 2 of 4 cases of recurring papilloma by the use of **radium**. He also removed by **excision** any recurring papillomas, the treatment averaging 2½ years. Plum (*Hospitaltidende*, Dec. 17-31, 1920).

MALIGNANT TUMORS.

The proportion of malignant as compared to benign growths, as shown by Semon's statistics, is about 1 to 7, but the fact that the former are more likely to be reported than the latter would tend to suggest that this proportion is fallacious. One malignant case in 20 would, judging from the specialists's average experience, probably be nearer the truth.

CARCINOMA.—Cancer of the larynx is somewhat more frequently observed in men than women, and, as is the case with this variety of growth in other parts of the organism, the majority of cases, about 66 per cent., are observed in subjects between the fortieth and sixtieth years. Cases are, though rarely, met with in children. Epithelioma is the variety usually observed, though all forms of cancer, even scirrhus, have been encountered in this situation.

Besides the symptoms observed in other forms of laryngeal tumor, hoarseness, dyspnea, cough, etc., glandular enlargement in the neck, and dysphagia usually appear, sometimes early in the history of the case. Pain,

another feature not complained of in benign tumors, is quite a prominent symptom and in some cases becomes intense and of a sharp, lancinating character. In the majority of cases it radiates toward the ear. The breath is fetid, the general health is undermined through general toxemia and deficient nutrition, and death usually occurs from exhaustion. In some cases, however, ulceration through the coats of a large artery may cause sudden death from hemorrhage; fatal pneumonia may be brought on by the aspiration of detritus, or asphyxia may be induced through the entrance into the laryngeal aperture of masses of food.

The laryngoscopic image afforded at first varies greatly in different cases and according to the location. It may at first resemble a benign tumor, and be taken for it; one cord may simply be enlarged, rounded at the edge, and slightly congested; a small ulcer, resembling an abrasion, may suggest syphilis, especially when the edges of the ulcer are sharp-cut and yellowish; a grayish projection or ulcer may suggest tuberculosis, etc. Elimination by examining the sputa for tubercle bacilli, or the administration of iodide of potassium, is often necessary in such cases to determine the true nature of the growth, and sometimes a small piece must be nipped off with forceps for microscopic examination. The development of the tumor is also irregular. Fungous masses, burrows, masses of necrosed tissue, and thick secretion, etc., make up a picture that is never forgotten when once seen.

The chances of recovery are absolutely *nil* when an early operation, including thorough removal of the

growth, cannot be carried out. When such a procedure can be resorted to satisfactorily the prognosis becomes comparatively favorable.

TREATMENT.—The safest rule as to the **extirpation** of laryngeal carcinoma resumes itself into instrumental methods whenever the case is seen near its incipency. If there appears, after careful examination, to be no peripheral involvement, and the growth is so situated that it can be, as it were, punched out with considerable surrounding tissue with special cutting forceps, this should be resorted to. An ulceration or thickening near or at the edge of a cord or a ventricular band may thus be enucleated. Such cases are unfortunately comparatively rare, and the laryngologist is usually consulted when the cancerous process has already advanced beyond this comparatively simple procedure. Excision then affords the only procedure capable of affording some chance of recovery. It is now advocated by most experienced laryngologists when the limits of the thyroid cartilage are not passed; that is to say, when only the tissues *within* the larynx proper are involved and when there is no glandular enlargement. Local applications of acids, cautery, arsenic, etc., but stimulate the development, and are therefore more hurtful than beneficial.

To assuage the sufferings of the patient, much can be done. The insufflation of **orthoform** or the local application of a **cocaine solution** before meals to the ulcerating tissues enables the patient to swallow his food. When he can no longer do this, a **stomach-tube** or a large rubber **catheter** may be introduced alongside the growth, into the pyriform sinus,

and the patient fed through it with **nourishing liquids**: milk and cream, soft-boiled eggs, broths, etc.

Tracheotomy, early in the case, when laryngectomy cannot be performed, by giving rest to the larynx seems to stay the progress of the growth. It should be performed low down. When the tissue involved includes only the soft structures, a **laryngofissure**, or **thyrotomy**, and **removal of the entire growth**, may give the necessary relief. When the disease is more extensive, but still confined to one side of the larynx, a **hemilaryngectomy** may sometimes be carried out with beneficial results. **Complete laryngectomy** has been resorted to with increasing frequency, and is strongly favored by some.

Out of 31 cases of **laryngectomy**, only 2 died soon after the operation (1 from lung abscess), and 11 were still well 1 to 9 years after the operation. Moure (Bull. de l'Acad. de méd., Mar. 1, 1921).

Report of 45 cases of **laryngofissure** without mortality, and with freedom from recurrence in 1 year in 37 cases, and in 3 years in 23 out of 29 cases. The author uses anesthesia by intratracheal insufflation of ether. He lays stress on persistent hoarseness from various causes as a precursor of cancer; on diagnosis through a laryngeal fragment obtained by direct laryngoscopy, and on endoscopy for settling the boundary of the tumor before laryngofissure. Chevalier Jackson (Ann. des mal. de l'or., etc., Dec., 1922).

Experience in over 100 cases confirmed the superiority of surgical treatment, provided **total laryngectomy** is practiced, with removal of the perilaryngeal infiltrations, of the affected lymphatic glands, and of the pharyngeal tissues involved. To facilitate speech after recovery, a phonation tube may be used. Leyro Diaz (Néoplasmes, Dec., 1924).

In intrinsic laryngeal cancer, early diagnosis should lead to **laryngofissure**, an operation which should be free from danger to life and followed by an adequate voice. In late cases, or if local recurrence takes place, a **partial laryngectomy** may be successful. Extrinsic cancer is seldom operable—through a lateral pharyngotomy. **Complete laryngectomy** is rarely helpful in extrinsic disease; it is occasionally indicated for neglected and extensive intrinsic cancer. Sir St. Clair Thomson (Arch. of Otolaryng., Jan., 1926).

Radium and the **X-rays** have been used by some, although the majority favor operation.

Radium is combined with laryngofissure by the writer, who has abandoned laryngectomy. He leaves 25 to 75 mgm. of radium in for 24 hours, and sometimes also uses the **X-ray**. Of 7 cases, all have remained well nearly 2 years or more. Sargnon (Arch. internat. de lar., etc., Dec., 1922).

Case in a man of 76, with glandular metastasis, who seemed completely restored to health by massive, **deep X-ray** treatment. Coleschi (Radiol. med., Dec., 1922).

The writer introduces **radium needles** of gold and a mixed alloy of nickel, silver, and steel, containing 7 to 12 mgm. of radium, inserted with laryngeal forceps at intervals of 6 to 8 weeks. An external **radium pack** of 100 to 200 mgm. at 1 inch distance is also used. Forbes (Jour. of Laryng. and Otol., Jan., 1923).

SARCOMA.—Sarcoma, according to Gurlt's statistics, occurs once in the larynx in every 848 cases of this form of tumor met with, while the general average of the cases reported by various observers would place the relative number of cases of laryngeal sarcoma as compared to laryngeal carcinoma at 1 in 23. It may be either primary or secondary.

It occurs in any part of the larynx, but with a predilection for the vocal

cords. The yellow color of sarcoma as compared to carcinoma, which is usually reddish at the start; the globular or rounded surface as compared to the ulcerative process observed early in the latter, and slower growth are important features, but the diagnosis should invariably be verified microscopically. The mixed forms are sometimes met with, *e.g.*, fibro-, myxo-, chondro-, angio-, adeno-, and melano- sarcoma. The subjective symptoms are not usually as severe; indeed, the patient may otherwise be in excellent health, as witnessed in a case seen by myself, and to all intents and purposes the case may simulate in this particular a benign tumor.

TREATMENT.—Early **extirpation** of the growth affords a far better prognosis than when carcinoma is present, since glandular involvement occurs later. When the tumor has involved the greater part of the larynx, **laryngectomy** should be resorted to. In inoperable cases **radium** and the **Röntgen rays** may be used to advantage. They are also used to prevent recurrence when extirpation has been resorted to.

INJURIES OF THE LARYNX.—

External injuries to the larynx may be the result of contusions, wounds of various sorts, and fractures. The symptoms produced are usually proportionate to the amount of damage done. Contusions may produce pain on speaking and swallowing, hoarseness, and aphonia, and on examination show redness and swelling, ecchymosis, or even a free hemorrhage. Punctured wounds of the larynx may produce marked dyspnea as the result of the compression of the trachea by an extensive cutaneous emphysema. Incised wounds may produce con-

siderable damage, according to the tissue or structure cut. In these cases the hemorrhage must be controlled and the danger of suffocation averted by **tracheotomy**.

Fractures are produced in a way similar to contusions, *i.e.*, by an external blunt force. The older the person, the greater the possibility of a fracture on account of the normal ossifying processes. The fracture usually occurs in the thyroid cartilage, and runs vertically. Flattening and broadening of the cartilage, displacement, or abnormal mobility and crepitus may be ascertained. **Ice** should be applied to control the swelling and the expectant treatment adopted.

Internal injuries to the larynx may occur from cauterization and scalding, unintentional operative lesions, and rupture and hemorrhage from muscular overstraining. The treatment depends upon the symptoms produced. The use of **menthol** pastilles or the instillation of a 10 to 20 per cent. solution of menthol in oil may have a beneficial effect when the larynx has been cauterized or scalded.

Military statistics show that laryngotracheal injuries are not frequent. Wounds of the neck may be taken as about 3 per cent. of the total wounds. In an experience with several thousand wounded the authors have found only about 30 wounds of the larynx and trachea.

The immediate results of laryngotracheal injuries are hemorrhage, emphysema, asphyxia, and sudden death. In the great majority of cases of penetrating wounds of the laryngotracheal tract, the respiration was compromised to such an extent that **tracheotomy** was necessary to save the life of the patient. Besides this preliminary preventive tracheotomy, the wound, as is the common practice in all war injuries, must be opened up

and cleaned and foreign bodies, etc., removed. These procedures constitute the immediate treatment.

The results consecutive to laryngo-tracheal injuries are classed by the authors as: (1) edema of the laryngeal mucosa; (2) suppurations; (3) inflammatory stenoses; (4) paralyses. Such results may necessitate a second tracheotomy. This should be systematically performed. Inter-cricothyroidean laryngotomy ought never be done, according to the opinion of the writers. Moure and Conuyt (*Revue de chir.*, xxxv, ii sem. i, 1916).

LARYNX AND TRACHEA, SURGERY OF.

THYROTOMY.—Thyrotomy is calculated to expose freely the interior of the larynx for the removal of foreign bodies and tumors. To admit air into the respiratory tract, however, in diphtheria, laryngeal edema, etc., it is not satisfactory, as a rule, being too close to the lesion for the relief of which it is practised. When a foreign body is impacted above the vocal cords and cannot be removed from above, it not only facilitates breathing, but also the removal of the offending mass. Tumors of the larynx, when situated within the larynx proper, are brought within easy access, and may be thoroughly scraped off.

The operation consists in a vertical incision through the skin in the median line and splitting of the thyroid cartilage underneath. Care should be taken to open the latter at the junction of the two alæ, as either cord may be injured if the median line is not closely followed. A sharp and strong bistoury is required. In some cases the cartilage is ossified and a fine saw must be employed. The operation is comparatively bloodless.

There is always danger of impair-

ing the voice, and it is advisable to close the wound as early as possible and with the utmost care, so that the vocal cords will be in the same relative position as before the operation. Some operators, when the larynx has been cleared of tumors, and when air must be artificially admitted into the trachea, extend the incision, performing a laryngotracheotomy in addition to the thyrotomy; close up the thyroid wound, and insert the tube below.

LARYNGOTOMY.—In case of emergency—*i.e.*, when, through the presence of a foreign body, an injury, edema, etc., air must artificially be admitted into the larynx—this operation is very satisfactory. It consists in an incision through the cricothyroid membrane in the median line from the thyroid cartilage down to the first tracheal ring. After incising the skin and on reaching the cricothyroid membrane beneath, an artery—the cricothyroid—is met with; this should be pushed aside and the membrane incised perpendicularly. In doing this, care should be taken to penetrate the tracheal mucous membrane, which tends to become detached and sacculated, thus blocking the trachea. A small tracheotomy tube should be used, and removed as early as practicable, necrosis of the cricoid or thyroid cartilages being otherwise likely.

LARYNGOTRACHEOTOMY.—When in laryngotomy the operation is extended so as to include the cricoid cartilage and the first ring of the trachea—not lower, lest the isthmus of the thyroid body be encountered—the procedure becomes a *laryngotracheotomy*. When the patient is on the verge of asphyxia, technical nicety must sometimes be sacrificed to the urgency of the case. The trachea

must immediately be opened, whether hemorrhage be feared or not, by a perpendicular incision in the skin and one a little shorter through the walls of the trachea. If nothing but a pen-knife is at hand, this may be used when cleansed, and two hairpins bent flatwise into letters S may be employed as hooks to keep the wound gaping while the patient's respiration becomes normal. Before incising the skin, however, it is always well to trace lightly, with a soft pencil, the site of the incision: *i.e.*, the middle line. If this precaution is neglected, the incision is almost always irregular; indeed, the knife may not enter the trachea at all, but suddenly plunge to one side of it. When the outline of the incision is drawn, the skin should be held firmly down in its proper place with the thumb and middle finger of the left hand, while the right does the cutting. The isthmus of the thyroid should be avoided if possible, but this is often difficult, owing to the short distance between it and the cricoid cartilage above.

TRACHEOTOMY.—The various conditions in which this operation is indicated may be divided into three classes: 1. Those in which a morbid process suddenly or gradually reduces the laryngeal lumen and involves the probability of asphyxia, such as diphtheria, croup, edema, paralysis, malignant disease, etc. 2. Those in which physiological rest tends to reduce the activity of the morbid process and delay its progress, such as laryngeal tuberculosis and syphilis. 3. Those in which an impacted foreign body cannot be removed through the glottis.

This operation, though apparently easy, is by no means so in the first class of cases mentioned, owing to

rapid perpendicular motions of the trachea when violent efforts at respiration are made. In the second class there is, as a rule, no dyspnea; hence the operation, in a thin subject especially, is less difficult, since the trachea is quiescent except when the patient swallows. The same may be said of the majority of cases included under the third class.

Anesthesia for tracheotomy should be local. General anesthesia is dangerous.

Salt solution, freshly prepared, containing 0.1 per cent. of **cocain** is used in Jackson's clinic. The injection should be intradermic, not hypodermic. Beginning low, a small quantity is injected into the median line. The needle is withdrawn and inserted at the upper border of the wheal. The needle is again withdrawn and inserted at the upper border of the second wheal, and so on upward until the region of the thyroid cartilage is reached.

The operation is performed as follows: The patient is placed on a table and the shoulders are raised on a pillow so as to cause extension of the neck. With a blue pencil, a line starting from the cricoid 5 to 7 cm. downward, exactly in median line, is drawn—the tracing for the incision. This should include the skin and platysma. Blood-vessels should now be watched for, and, if any are met with, they should be tied if at all important, or pushed aside if possible. Working down, cutting only on the grooved director, and strictly following the axis of the trachea, the rings are soon reached. If the vessels have received proper attention, the wound should be comparatively dry. The tenaculum is then used to steady the trachea, and, an assistant holding the

lips of the wound apart with hooks, the first ring of the trachea and the cricoid being respected. A violent inspiration then occurs, followed by the sudden expulsion of mucus, blood, or diphtheritic membrane if any be present: a dangerous feature for the surgeon if he is not on his guard. At this time, the patient often ceases to breathe for several seconds. Though he practically always recovers, the opening should be carefully examined lest a mass of membrane, a plug of mucopus, or a foreign body be the cause of the arrest of breathing. If it is prolonged, artificial breathing should be resorted to, or the patient should be slapped on the back and suspended by the heels. Finally, as a rule, the patient takes a deep breath and the respiration continues normal. The cannula is immediately introduced, the sponges being taken off at the same time. The flow of blood ceases almost immediately upon the restoration of the normal breathing; for prudence's sake, however, the patient should be raised and leaned forward, so as to cause what blood might ooze from the wound to flow externally, instead of into the trachea. When the operation has been satisfactorily performed, the external wound above and below the tube is closed by universal suture clamps or regularly inserted sutures, care being taken to approximate and adjust the edges accurately. The lower end of the wound should remain open for drainage.

Keen introduces a silk suture into the trachea on each side of the incision and through the skin, ties the ends, and leaves them hanging long. This provides a permanent retractor with which the surgeon can at any

time open the trachea. If no tracheotomy tube is at hand, an elastic band tied around the neck can be used to connect the free ends of the ligatures, and so keep the trachea patent for free respiration.

Silver tubes are to be preferred when the instrument is to be worn a long time; aluminum tubes are the best when they are to be removed soon, since the metal is corroded by the secretions. The hard-rubber tubes are clumsy and become quickly saturated and foul. A double tube—the largest that can be easily accommodated—should always be employed. It should also be carefully tied with tapes, around the neck, particularly in children.

During the operation, and as long as the patient is confined to his room, generally about a week, the atmosphere should be kept at a temperature of not less than 80° F. (26.7° C.), and maintained in a moist state by means of steam, obtained by boiling water in the apartment. In short, the object should be to furnish the lungs with air possessing as nearly as possible the properties it would possess if it were inhaled through the nose. To further attain this object, the foreign particles floating in the atmosphere can be arrested at the mouth of the cannula by straddling a piece of thin muslin over it; care should be taken, however, not to attach it so as to interfere with the free discharge of mucus. The best means is to tie a thin muslin handkerchief around the neck above the cannula, letting it overhang its orifice. This not only prevents the ingress of dust during inspiration, but also serves to prevent the regurgitation of mucus, which often takes place without such a con-

trivance, when a coughing spell forces the discharges up to the mouth of the tube.

An important point is to keep the cannula as free as possible from the copious discharges which are formed for a couple of days after the operation. An intelligent attendant should be carefully instructed to withdraw the inner cannula every two hours, to cleanse it carefully with hot water, then to reintroduce it into the outer tube after having effectively freed the cavity of the latter of any mucus that might have accumulated there. This may be done by means of a feather, a piece of sponge, or absorbent cotton securely and tightly fastened to a suitably bent piece of thin brass wire.

The patient should be provided with two complete cannulas so as to occasionally be able to withdraw the outer tube also and cleanse it thoroughly. This can be done after a couple of days, the wound having had time to assume the shape of the outer cannula, thus enabling it to remain patulous for a short time after the instrument has been withdrawn complete. The extra cannula, previously warmed to avoid exciting cough, should be introduced immediately upon the withdrawal of the other, using, to assist its entrance, a Cohen pilot. This instrument, introduced into the outer cannula, presents a blunt-pointed knob which separates what tissues might impede the progress of the latter. It should, of course, be instantly withdrawn as soon as the tube is in position. The occasional (once or twice a week after the first few days) withdrawal of the tubes serves also to avoid what danger the corrosion of a metallic cannula might incur. Cases have been reported in

which pieces of such a cannula, broken off at an eroded point, occasioned alarming symptoms.

Occasionally, granulations are formed at the external tracheal orifice, and in the trachea itself, the latter being especially the case when a fenestrated tube is employed. Strong astringent solutions sometimes suffice to destroy them; in some cases, however, surgical measures are necessary.

When the cannula is to be withdrawn permanently, the natural breathing powers of the patient should be tested by closing the aperture of the cannula with a stopper. If this is borne without difficulty, the instrument may be withdrawn, but kept within easy reach, with pilot in position, for sudden replacing if necessary. As a rule, however, this is not required, and the wound closes up after a few days to finally heal completely a week or two later.

The cannula has occasionally to be worn permanently, the patient, to speak, being obliged to place his finger upon the external opening. In this case Luer's tracheotomy tube, the inner cannula of which contains a silver pea, whose object is to arrest the expired current of air, so as to enable it to pass between the vocal bands, will be found very useful, rendering the use of the finger to close the tube unnecessary.

PARTIAL LARYNGECTOMY is a more extensive operation than thyrotomy. In addition to the growth and the involved soft tissue, a portion of the cartilaginous framework is likewise removed.

Partial laryngectomy is indicated when malignant growths are limited to one side and there is every reason to suspect that the cartilaginous and

the deeper structures are also involved in the process.

COMPLETE LARYNGECTOMY is performed only when the malignant disease is so extensive that relief cannot be secured from the simpler and less radical measures. Even should the patient recover from the operation, the condition of the individual without his larynx is a pitiable one.

After the usual preparation, the patient is placed in the Trendelenburg position, a preliminary tracheotomy performed, and the administration of the ether continued by the insufflation method. Following the incision in the median line, the soft structures are separated from the larynx as far as the anterior wall of the esophagus. A heavy anchor suture is passed through the first and second tracheal rings on either side and fastened to the skin to prevent the trachea from falling into the mediastinum. The trachea is then severed from the cricoid ring with a sharp scalpel, and its posterior surface from the esophagus with the finger or a blunt instrument as far as the arytenoid cartilages, when it is severed by a transverse incision. The wound in the anterior pharyngeal wall is closed by suturing together the lower pharyngeal and the thyrohyoid membranes. After closure of the skin incision, a thin piece of moist gauze is placed over the tracheal stump, which has been securely fastened to the skin, to moisten and filter the inspired air. The foot of the bed is elevated until the pharyngeal wound is healed and the patient can take food by the mouth. This is usually in about four days. In the mean time he is fed by the rectum.

Attempts have been made, with some success, to enable laryngectomized

patients to speak, either with an artificial larynx, or by the use of the "esophageal voice," the mouth of the esophagus forming a pseudo-glottis, through which air is propelled from the esophagus and stomach.

WILLIAM A. HITSCHLER,
Philadelphia.

LAUDANUM. See OPIUM.

LAVAGE OF THE STOMACH.—By this is meant washing out the stomach with water or other fluids through a stomach-tube or catheter and then siphoning it off. Performed with proper precautions, this therapeutic procedure is both useful and devoid of danger.

APPARATUS.—An ordinary siphonage apparatus should be employed, as it is less liable to injure the gastric mucosa than the stomach-pump. A soft-rubber stomach-tube is attached by means of a small length of glass tubing to a piece of rubber 2 or 3 feet long into the free end of which is inserted a glass funnel holding about a pint. The stomach-tube, about 30 inches (75 cm.) long and from $\frac{1}{4}$ to $\frac{1}{2}$ inch (6 to 12 mm.) in diameter, should have a closed tip and two fairly large lateral openings (to give passage to solid particles of food) as near as possible to the tip; on the tube should be a mark indicating the distance from the upper incisor teeth to the stomach.

For use in infants a soft-rubber catheter (16A—24F) provided with a large lateral fenestra and joined by glass connection to 2 feet (60 cm.) of rubber tubing, to which an 8-ounce (240 c.c.) glass funnel is attached, is desirable. A mouth gag may also be required.

Before and after using, the whole apparatus should be cleansed by allowing it to lie in an antiseptic solution and afterward rinsing in lukewarm sterile water.

SOLUTIONS.—For removing mucus from the stomach an alkaline mineral water (Carlsbad, Vichy), Carlsbad salt solution (1:250), or a solution of sodium bicarbonate (1 to 5 per cent.) may be employed at a temperature of from 90° to 100° F. (32° to 38° C.). Not more than 1 pint (500 c.c.) should be introduced at

a time, since more might overdilute the stomach. The lavage is repeated until the stomach contents return clear, unless the patient's condition prevents.

TIME FOR LAVAGE.—The best time for lavage is in the morning before the first meal; but if the patient's distress demands, it may be done three or four hours after the last meal. In severe cases both morning and evening lavage may be necessary.

TECHNIQUE.—The patient sitting in a chair or semiupright in bed, with his head bent slightly forward (to allow saliva and vomitus to escape from the mouth), faces the operator. A child may be held by a nurse in the same position. If gagging is excessive, brush or spray the throat with a 5 per cent. solution of cocaine. All dentures (artificial-tooth plates) should be removed, and the chest and lap protected by a large towel or apron. A small basin in the patient's hands will be necessary to receive any saliva or vomitus. Moisten the tube with glycerin or water and pass it along the roof of the mouth until the esophagus is reached. Instruct the patient to swallow, and the tube will be carried on into the esophagus, when the tube is then rapidly pushed on into the stomach. If the stomach contents do not immediately appear in the funnel the latter should be lowered and the contents siphoned off. Slight epigastric pressure may be required.

Having removed the stomach contents or been assured that the viscus is empty, pinch the tube close to the patient's mouth, elevate the funnel slightly, and fill it with the solution. Remove the compression from the tube and allow almost all the contents of the funnel to flow into the stomach, reserving sufficient fluid to start the siphonage. The stomach contents are then siphoned back into the funnel, by lowering the latter, and are discarded, taking care to see that approximately the same quantity that was introduced returns. This process is repeated several times, and it is desirable that the patient move about and change his position to a recumbent one, that all portions of the stomach may be reached and cleansed of its mucus.

The tube is removed, by allowing a

small quantity of fluid to remain in the funnel, and, as the tube is slowly withdrawn, this is allowed to drain back into the stomach until the tube is in the esophagus. Then pinch the tube tightly to prevent the solution from escaping into the larynx or mouth. The tube must not be removed from the stomach empty, as the mucous membrane may be sucked up into the openings of the tube and suffer laceration or injury.

In the insane or in unruly children the tube may be passed through one of the nostrils, but in this case a smaller tube must be employed and it must be well lubricated. W.

LEAD.—Metallic lead (plumbum) is not official, as it is not employed in medicine. Lead combines with oxygen to form oxides, one of which (the yellow) is official as well as with the acids and with chlorine, iodine, bromine, etc., to form salts. Of these salts the acetate is alone used internally to any extent, although the iodide has also on rare occasions been employed for alterative purposes.

PREPARATIONS AND DOSE.—*Plumbi acetas*, U. S. P. (lead acetate) $[(CH_3.COO)_2Pb + 3H_2O]$, occurs in colorless, shining, transparent but efflorescent, prismatic crystals or in heavy, white masses, having a slightly acetous odor and a sweetish, astringent, and later metallic taste. It is soluble in 1.4 parts of cold and $\frac{1}{2}$ part of boiling water, in 30 parts of cold alcohol and 1 part of boiling alcohol, in 3 parts of chloroform, and in 5 parts of glycerin. Dose, 1 grain (0.06 Gm.).

Plumbi iodidum, U. S. P. VIII (lead iodide) $[PbI_2]$, occurs as a heavy, bright-yellow, odorless and tasteless powder, which is permanent in the air. It is soluble only in about 1300 parts of cold water and in 200 parts of hot, very slightly soluble in alcohol, but soluble in solutions of the fixed alkalies, of

potassium iodide, and of sodium thio-sulphate. Dose, 1 grain (0.06 Gm.).

Plumbi monoxidum, U. S. P. (lead monoxide; litharge) [PbO], occurs in a heavy, odorless, tasteless, yellowish or reddish-yellow powder, practically insoluble in water and insoluble in alcohol, but soluble in acetic or dilute nitric acid and in warm solutions of the fixed alkali hydroxides.

Liquor plumbi subacetatis, U. S. P. (solution of lead subacetate; Goulard's extract), is a liquid containing in solution lead subacetate [approximately $\text{Pb}_2\text{O}(\text{CH}_3\text{COO})_2$] corresponding to not less than 18 per cent. of Pb and is made by adding a solution of lead acetate to powdered lead oxide and boiling.

Emplastrum plumbi olcatis, U. S. P. (lead plaster; diachylon plaster), is made by heating 1000 Gm. each of olive oil and lard until liquefied, adding 1000 Gm. of lead monoxide and mixing thoroughly, adding boiling water, 350 c.c., and boiling and stirring, with further additions of water, until the mass is homogeneous and is pliable and tenacious when dipped in cold water. Used externally.

Unguentum plumbi oleatis, U. S. P. (ointment of lead oleate, formerly diachylon ointment), is made by melting 50 parts of lead oleate plaster and 49 parts of white petrolatum, straining, allowing to cool, adding 1 part of oil of lavender, and stirring the ointment until it congeals. Used externally.

Plumbi nitrates, U. S. P. VIII (lead nitrate) [$\text{Pb}(\text{NO}_3)_2$], occurs in colorless and transparent or white and nearly opaque crystals, odorless, with a sweetish, astringent taste, and permanent in the air. It is soluble in 1.85 parts of water, but almost insoluble in alcohol. Used externally.

Emplastrum saponis, N. F. (soap plaster), is made by incorporating 1 part of soap, previously rendered semi-fluid with water, with 9 parts of melted lead oleate plaster. Used externally.

Liquor plumbi subacetatis dilutus, N. F. (diluted solution of lead subacetate), is made by dilution of Goulard's extract and contains about 1 per cent. of lead subacetate. Used externally.

Ceratum plumbi subacetatis, N. F. (cerate of lead subacetate; Goulard's cerate), is made from 20 parts each of solution of lead subacetate, wool fat, and white wax, 38 parts of white petrolatum, and 2 parts of camphor. Used externally.

Unguentum plumbi iodidi, N. F. (ointment of lead iodide), contains 10 per cent. of lead iodide. Used externally.

Lotio plumbi et opii, N. F. (lead and opium wash), consists of 1.75 parts of lead acetate, 3.5 parts of tincture of opium, and water enough to make 100 parts. Used externally.

Pilula opii et plumbi, N. F. (pill of opium and lead), contains 1 grain (0.06 Gm.) each of powdered opium and lead acetate. Dose, 1 pill.

PHYSIOLOGICAL ACTION.—

Lead applied locally acts as an astringent, causing a precipitate of albumin so dense that the underlying tissues are protected from the entrance of the metal and of any other irritants that may be present. The relative absence of corrosion from lead is due both to this fact and that lead forms insoluble and consequently non-irritant salts with the strongly corrosive sulphuric and hydrochloric acids. Concentrated solutions of lead salts are, however, capable of inducing local inflammation. There is reason to believe that lead may be absorbed from the unbroken skin.

Taken internally in therapeutic doses, lead likewise acts as an astringent, and tends to diminish the secretions of the gastrointestinal tract. Beyond these effects the manifestations are those of poisoning—especially where the drug enters the system continuously in small doses, large single doses usually causing no symptoms indicative of absorption of the drug. The nitrate, the subacetate, and the acetate are poisonous in the order named.

ACUTE LEAD POISONING.—

Acute poisoning is rare, but may occur when a soluble salt (notably the acetate) is taken in massive amounts (not less than 1 ounce is necessary to produce serious effects). The symptoms are a sweet, metallic taste in the mouth, pain in the epigastrium, and vomiting of white, milky-looking liquids or white curds, mixed with food if any food was present in the stomach. The white color indicates the presence of lead chloride, formed by interaction with the hydrochloric acid of the gastric juice. Later, irritation of the intestinal tract occurs, with an increase of pain and either diarrhea due to gastroenteritis or, in some cases, obstinate constipation is noticed. The stools are at times black in color, from the action of the intestinal hydrogen sulphide, which forms lead sulphide. The pulse in the more serious cases becomes rapid and tense, later weak and compressible. The face is anxious and may be either pale or livid. Excessive thirst is present, with cramps in the calves of the legs or muscular twitchings.

In fatal cases coma, epileptoid spasms, or collapse ensues. Up to the point of reflex (irritative) involvement of the nerve-centers (spasm, coma, or collapse) the prognosis is good; beyond this it is unfavorable.

Treatment of Acute Lead Poisoning.—If there is reason to believe that any of the lead salt is present in the stomach, the stomach siphon may be used. Any **soluble sulphate**, *e.g.*, **magnesium sulphate** or **sodium sulphate**, will decompose the lead salt and form an insoluble sulphate of lead; if used in excess the salts mentioned will act as purges and wash out the offending matter. If a sulphate be not available, **white of egg** or **milk** may be used. Cramp and spasms may be relieved by **hot applications** to the abdomen and to the extremities. Pain may be relieved by **opiates**.

In acute plumbism the writer urges care that the clothing worn during the attack be entirely free of lead. The skin should be cleansed by a **full bath with friction** or by successive **local washings**. **Mouth washings**, careful **cleansing of the teeth**, and **irrigation of the nasal cavities** with warm **saline solution** are indicated. Prompt arrest of the colic with **amyl nitrite** or **nitroglycerin** may be attempted, with subsequent use of **erythrol tetranitrate** or **sodium nitrite**. The nitrites are merely auxiliaries of **atropine** and **morphine**. Removal of the bradycardia during lead colic was observed by the writer under moderate doses of **belladonna** tincture. Where the pronounced analgesic action of morphine is no longer essential, **papaverine sulphate**, $\frac{3}{4}$ grain (0.04 Gm.), may be used to relax the intestinal spasm. Constipation is often, in the severe cases, best treated at first by daily **colonic injections of warm water**, purgatives by mouth increasing nausea and vomiting. Later, the bowels should be caused to act at least once and preferably 2 or 3 times daily. For elimination by diaphoresis a full dose of **sweet spirit of niter** 3 times, and later twice, a day is effectual. L. T. de M. Sajous (N. Y. Med. Jour., Mar. 10, 17 and 31, 1917).

CHRONIC LEAD POISONING.

—The sources of poisoning by lead are very numerous. Occupations in which lead is employed, however, predominate as causative factors, and painters, white-lead-paint mixers or grinders, wall- and other paper- mill operators, glaziers, plumbers, electricians, type-setters, etc., are the victims in the great majority of cases.

Adulterated foods and liquids represent the main sources of poisoning among those whose occupations do not involve exposure. Cooking utensils painted white inside, bread made of flour contaminated with a lead-filled grindstone, cake colored with lead bichromate to avoid the use of eggs, imperfectly burnt pottery, fruit-jars glazed with lead, tins of meat closed with it, etc., are many media through which lead can reach the system. A fruitful cause of poisoning is water conveyed through lead pipes, the lead being slowly dissolved. When, however, the water contains even a minute quantity of lime salts, an insoluble coating is formed which arrests all further action as soon as the inside of the pipes is completely covered. Cosmetics, hair-dyes, face-powders, and leaden toys occasionally cause plumbism. Lewin has observed many cases from swallowed shot, holding shot in the mouth, inhalation of lead-laden air, lodged bullets, etc.

Constitutional Effects.—Slow absorption of lead, whether due to industrial or accidental causes, mainly affects the muscles, the peripheral nerves, the liver, and the kidneys. The symptoms vary considerably in different cases. Pallor of muscles and mucous membranes is an early result, fibrosis occurring in advanced cases, accompanied by degenerative changes in the nerve-endings. These changes become less

marked as the spinal centers are approached, the spinal cord being usually normal. The brain, however, is not so exempt from morbid changes, periarteritis being the chief pathological change caused.

A blue line along the margins of the gums, at the base of the teeth, is an important sign. It is especially marked in persons who are not cleanly as regards their mouths, and is due to precipitation of lead sulphide by the hydrogen sulphide set free through the activities of bacteria. Anorexia, nausea, metallic taste, and fetid breath are other common symptoms.

Anemia.—Destruction of red cells to an excessive extent is believed to occur in lead poisoning. Jaundice and a deeply pigmented urine may result. A characteristic condition of the erythrocytes is that of "basophilic degeneration," which consists in the presence in these cells of granules staining with basic dyes, and is often among the earliest manifestations of lead poisoning. According to Schmidt, more than 100 granulated reds per million points to lead poisoning, the number usually ranging between 300 and 3000.

In 381 lead workers, the following blood changes were found:

Pallor of red cells	71 per cent.
Anisocytosis	44 " "
Polychromatophilia	40 " "
Stippling (basophilic degeneration)	39 " "
Poikilocytosis	23 " "
Nucleated red cells	8 " "
Mycelocytes (eosin)	2 " "

Too little emphasis has been placed upon the blood picture as a whole. The average red cell count was 4,000,000, and the hemoglobin, 79 per cent. The significant thing is the presence of the serious cell changes above listed, in conjunction with only a slight reduction of red cell count and

hemoglobin. M. R. Mayers (Indust. Hyg. Bull., N. Y. State Dept. of Labor, July, 1926).

About 40 per cent. of the leucocytes may be mononuclears, even in incipient cases. The writers found basophilic granules in 50 per cent. of all exposed subjects, with or without symptoms of plumbism. Examination of the urine for lead is important for early diagnosis, but is a tedious procedure. Lead may also occur in the spinal fluid. Heim, Agasse-Lafont and Feil (Bull. méd., Mar. 18, 1922).

Weakness, lassitude, amenorrhea, and abortion are among the accompaniments of saturnine anemia.

Lead Colic.—This symptom is most frequently met with in painters who mix and use white lead. The abdominal cramp is usually very severe, the muscles being rigid and contracted. A peculiarity of the pain is the fact that the location of its greatest intensity is usually around the umbilicus. It occurs in accesses, often accompanied by nausea or vomiting. Relief is frequently procured by exerting pressure upon the umbilical region. The tongue is white and contracted and there is thirst, which is sometimes intense. Obstinate constipation is the rule. The face is pale or jaundiced. The pulse is slow and firm, and the rate of respiration may be increased. Vascular spasm is believed to exist both during the attacks and in the intervening periods, and the blood-pressure is, as a rule, high. Parotiditis may also occur.

Tanquerel des Planches, among 1179 patients with lead colic, observed a heart rate of 20 to 60 a minute in no less than 678 cases.

After continuing for a period varying from a few hours to several days, the symptoms gradually recede and the access ceases. When no treatment is resorted to and the causative occupation is

continued, the attacks return frequently, and death may finally occur through cachexia or anemia, paralysis of the respiratory muscles, chronic nephritis, cirrhosis of the liver, or through some intercurrent disorder.

In 16 patients with old embedded leaden projectiles, unaccountable symptoms had been observed—hypertension, albuminuria and casts, constipation, colic, and anemia. The urines showed lead in 6 of the 16 to the amount of 0.5 to 1 mg. per liter of urine, or an excretion of more than 1 mg. daily. The intestinal and nervous symptoms could not be relieved, but in 3 cases the albuminuria disappeared completely within 2 to 3 weeks after removal of the lead bullet. Loeper and Verpy (*Progrès méd.*, xl, 81, 1916).

Lead Paralysis.—In the cases developing slowly, paresis of various systems, central and peripheral, frequently occurs, the most characteristic of these being wrist-drop, usually bilateral, due to paralysis of the extensor muscles of the forearm, the supinator longus, however, generally remaining normal. The causative condition is a peripheral neuritis, though the anterior horn cells are sometimes secondarily involved. Anesthesia may temporarily accompany the paralysis. More frequently there are sharp joint pains (lead arthralgia).

Weakening of the extensors of the hands pointed out as a common and at times the only evidence of lead poisoning. A pale complexion is also of significance. Teleky (*Münch. med. Woch.*, Feb. 29, 1924).

Vertigo, loss of memory, disturbances of the special senses (amblyopia), cerebral palsies, hemiplegia, and monoplegia have also been noted.

Lead Encephalopathy.—In occasional cases marked cerebral symptoms occur. These may develop gradually or quite suddenly, violent headache, ver-

tigo, tinnitus, strabismus, and other cerebral manifestations presenting themselves. Convulsions, amaurosis, delirium, and coma, or a condition simulating epileptic fits, hallucinations, mania, melancholia, and hysteria are at times met with. Saturnine epilepsy usually ends in death. According to Oliver, alcoholism predisposes to lead encephalopathy.

Case of acute lead encephalopathy in a man who had worked as a glost kiln placer in a pottery for 6 years without any evidences of lead intoxication other than a lead line. Suddenly he developed pallor, weakness of the arm muscles, general asthenia, tremors of the tongue and fingers and nervous excitability. Two weeks later, he became unconscious for an hour. This was followed by severe headache, ptosis and diplopia. Almost complete recovery resulted after 6 months' treatment. M. D. Shic (Jour. Amer. Med. Assoc., Aug. 23, 1924).

General Disorders Due to Lead.—

Lead may act as an etiological factor in many diseases, *e.g.*, arteriosclerosis and gout. Its rôle as such is fully considered in the articles upon the various affections in which it is concerned.

Among 274 cases of lead poisoning, the writer found renal disturbance in 178. Transient appearance of albumin, casts and sometimes kidney cells may be the first sign, or it may accompany lead colic. When these evidences persist a change of occupation should be insisted on. Gigliolo (Jour. Amer. Med. Assoc., July 28, 1917).

A study of the behavior of "tetra-ethyl lead" and "ethyl" gasoline directed attention to the possibilities of absorption of lead through the sound skin. In animals, such absorption of ethyl gasoline could be secured. Thus far, cases of lead poisoning have not been found at filling stations or garages. The time between a man's exposures to lead may be long enough to permit apparent good health though he may

be storing lead. It may take years before he stores enough or before a sufficient change takes place in his metabolism to cause lead symptoms. F. B. Flinn (Jour. Industr. Hyg., Feb., 1926).

Treatment of Chronic Poisoning.

—The indications are to remove the causes, as well as the poison already in the body, and to treat the lesions or tissue-changes produced by the poison. Frequent doses of **magnesium sulphate** will not only relieve the colic but will convert any lead present in the gastrointestinal tract into an insoluble sulphate, and cause its expulsion from the body. Deléarde recommends **saline hypodermoclysis**, and Mattirlo administered $\frac{1}{2}$ grain (0.03 Gm.) of **erythrol tetranitrate** in a high-tensioned case with benefit. **Jalap** and **calomel**, guarded with **opium** to prevent griping, and **alum** in 2-grain (0.12 Gm.) doses with **opium** or **morphine**, are suggested. Where a saline purgative to relieve constipation cannot be used because of vomiting, large **enemas** may be employed. When cerebritis is present a **blister** may be applied to the nape of the neck, and **amyl nitrite** and **sweating** (by **pilocarpine**) may be tried.

Two cases of lead colic in workers on brass containing 1 per cent. of lead. Prompt benefit was derived from a suppository with 0.0005 Gm. ($\frac{1}{20}$ grain) of **atropine**. Use of 1 or 2 such suppositories suggested in all cases of lead colic. Althoff (Münch. med. Woch., Mar. 11, 1913).

In lead colic the author at once gives 1 or 2 hypodermic injections of **morphine**, to relieve pain and calm excitement. On the second day, **atropine sulphate** is given hypodermically, at first $\frac{1}{20}$ grain (0.0005 Gm.), morning and evening, later three times a day. In some cases **fomentations** are applied to the abdomen; in others **ice poultices** are used.

By this treatment the colic is relieved. The vomiting ceases on the third or fifth day in severe cases; in milder ones it is relieved immediately, and small quantities of milk and water are allowed. Half a gram ($7\frac{1}{2}$ grains) of powdered **scammony** is then given as a laxative.

As a result of the administration of atropine, spasm of the intestines abates and a light purgative is sufficient to bring about evacuation of the bowels. Albert Mathieu (Paris méd., Nov. 1, 1913).

To eliminate the lead the sheet-anchor is **potassium iodide**, given in doses of 10 to 20 grains (0.6 to 1.2 Gm.) three times daily. It is believed that a double soluble salt (potassic iodide of lead) is thus formed, which may be excreted by the kidneys through the urine and by the liver through the bile. **Hot baths** and **diuretics** may be ordered to promote elimination. Paralysis is an indication for the exhibition of **strychnine** in large doses, during treatment with potassium iodide (given separately), and the employment of **massage** and **electricity**. The induced (faradic) current should be employed if the muscles react; if they do not, the galvanic current is indicated. When no reaction to the direct (constant or galvanic) current is observed, the paralysis is seldom recovered from. In arthralgia and lead encephalopathy **opium** or **chloral hydrate** may be required.

In all cases **removal from the source of poisoning** should be insisted upon and a strengthening diet ordered. **Iodide of iron** is recommended for the anemia.

Iodine seems to lose its efficiency in hastening lead elimination when it is given for a material time. This can in a measure be overcome by giving an intravenous injection, in

one of the veins of the arm, of 3 grains (0.2 Gm.) of **sodium iodide**. By mouth the author generally uses also sodium iodide, but sometimes alternates it with the **potassium salt**. The iodide should be given at first in 3-grain (0.2 Gm.) doses in a glass of milk or water, on an empty stomach, three times a day, to be followed at night by $\frac{1}{2}$ to 1 ounce (15 to 30 Gm.) doses of a saturated solution of **magnesium** or **sodium sulphate**, well diluted. Large quantities of milk or water should be taken throughout the day. A weekly urinary analysis is imperative, and if the elimination of the toxic material decreases an increase is made in the iodine salt, given even up to 60 grains (4 Gm.) daily.

For the constipation, no remedy compares with **alum** when colic is present:—

R. *Alum* 3ij (8 Gm.).

Diluted sulphuric acid. 3j (4 c.c.).

Distilled water,

Syrup of orange

flowers of each 3ss (15 c.c.).

M. Sig.: A dessertspoonful (10 c.c. — $2\frac{1}{2}$ drams) every four hours in hot water.

For wrist-drop or other local manifestations of nervous involvement, the author injects **strychnine**, employs daily **massage** of the parts, and also uses **passive hyperemia**, applying a rubber bandage 10 feet long around the upper arm, where it should be allowed to remain at least thirty minutes. After its removal the forearm is soaked in **hot water**, and is then ready for **galvanic electrical treatment**. A. F. Stuart (N. Y. Med. Jour., Feb. 27, 1909).

Sweat baths with or without the use of **sulphides** are useful in lead poisoning. A **sulphur bath** may be obtained by dissolving 6 ounces (180 Gm.) of **potassium sulphuret (sulphide)** in half a tubful of water. Above all, daily physical work, preferably out of doors, favors elimination. Fantus (Ill. Med. Jour., May, 1910).

Employment of **electrolysis** or **de-ionization** in incipient industrial lead poisoning advocated. Double (arm-and-leg) baths were used, the arms being placed in one bath, the legs in the other, and the current thereby made to pass through the whole body. The bath was given daily or every second day, at 16 volts and 20 to 40 milliamperes. The positive pole was placed in the foot bath and the negative in the arm bath. If the current is introduced gradually by a suitable rheostat no shock is felt. The resistance of the bath water is reduced by adding common salt. Fourteen workmen especially pale and cachectic were treated, with marked resulting improvement. The blue line on the gums gradually faded away. Sir T. Oliver (Lancet, Aug. 23, 1913).

Calcium permanganate ($\frac{1}{4}$ gr. *t. i. d.*) is recorded to be of value by Stephens. A **fixation abscess** induced by **subcutaneous injections** of 1 c.c. of **turpentine** has resulted in marked improvement. G. A. Moleen (Amer. Jour. Med. Sci., Dec., 1913).

Some children with **pica** have a craving to gnaw painted objects and may thus become poisoned with lead. Symptomatic treatment of the spasms calls for **chloroform inhalations**; for the anemia, **iron** and **arsenic**; for the local palsies, **massage** and **electricity**, and for permanent palsies, **surgical measures**, if possible. Medicinal treatment for the removal of lead from the system consists of **potassium iodide**, 3 to 5 grains (0.2 to 0.3 Gm.) 3 times daily, with a morning purge of **magnesium sulphate**. J. C. Ruddock (Jour. Amer. Med. Assoc., May 24, 1924).

Decalcifying agents have been shown to increase the output of lead. Conversely, conditions favoring calcium retention tend toward a complete storage of lead in the bones. Therefore, during periods of danger it is well to facilitate storage of lead by the ingestion of ample **calcium**, rather than to set the lead free. After the acute toxic manifestations have passed, elimination of lead may be accelerated by a low intake of calcium, **acids** and their

ammonium salts, **sodium bicarbonate** and **potassium iodide**. Caution should be exercised, however, in applying these measures in nephritic patients. Aub, Fairhall, Minot and Reznikoff (Medicine, Feb.-May, 1925).

THERAPEUTICS.—Aside from Bell's attempts at the treatment of cancer with lead (see **CANCER**), lead is not given to affect the system at large. It is used for the local effects, which differ according to the form used. Lead acetate is an astringent remedy sometimes used to arrest **hematemesis**, especially when due to **gastric ulcer**. It is also recommended in **chronic gastritis** with **pyrosis** and **gastralgia**. In the **diarrhea of phthisis** and in **summer diarrhea** a few grains of the acetate, with a small dose of opium or morphine, not infrequently bring relief. In **acute** and **chronic dysentery** an enema of 4 grains (0.25 Gm.) of the acetate, $\frac{1}{2}$ grain (0.03 Gm.) of morphine acetate, and 1 ounce (30 c.c.) of warm water is useful to relieve the tenesmus and reduce the frequency of the stools.

In **cholera** and the purging from **dysentery** and **typhoid fever**, a few grains of the acetate may be combined with starch and a moderate dose of opium, and be given in an enema. If it is to be taken internally, pills should be prescribed, to defer its action until it has entered the intestine. The acetate may also be combined with opium in suppository for checking various forms of **diarrhea** and for the relief of **irritable conditions of the rectum**.

Externally, an excellent application to **burns** is white-lead paint (lead carbonate and linseed oil), especially if the surface is not very large and there are no fears of excessive absorption of the lead.

Lead lotion (liquor plumbi subacetatis), diluted with 3 or 4 parts of water, is a good application in **eczema** where there is much weeping. Its use in combination with laudanum (lead water, 4 parts; laudanum, 1 part; water, 16 parts) has long been a favorite measure in the treatment of **inflamed surfaces, bruises, sprains, fractures, blisters, scalds, excoriations, and fissured nipples.**

Lead acetate is a useful application for the **dermatitis** produced by **poison-ivy** (*Rhus toxicodendron*), as the lead precipitates the non-volatile oil of the poison. For this purpose Hare advises that 8 grains (0.5 Gm.) of lead acetate be dissolved in a pint (500 c.c.) of alcohol and used as a wash; cooling applications should follow, but ointments should be avoided, as they dissolve the poisonous oil and spread the irritation.

In **pruritus vulvæ** lead water or cerate may be used locally. Helva recommends the application of equal parts of lead plaster and linseed oil for **sweating feet**. They should be applied on linen, wrapped around the feet every third day. Powdered lead nitrate is useful in **onychia**.

In **gonorrhea** and **leucorrhea** a solution of lead acetate (3 or 4 grains—0.2 or 0.25 Gm.—to the ounce—30 c.c.—of water) may be used as an injection. Lead preparations should never be used in eye lotions, as they are apt to deposit the lead in the tissues of the cornea and leave permanent white patches, especially if ulceration of the cornea be present.

C. E. DE M. SAJOUS

AND

L. T. DE M. SAJOUS,
Philadelphia.

LEECHING.—This procedure is resorted to for the abstraction of blood from congested areas inaccessible to wet cups.

Two varieties of natural leeches are available: the small American leech, which has a capacity of about a dram (4 c.c.) of blood, and the Swedish leech, the capacity of which is three or four times as great. One to 6 leeches may be applied at one time if desired. They should, however, never be applied to regions supplied with much loose connective tissue (eyelids, labia, scrotum, or penis), as extensive ecchymosis may result. They should not be applied directly to an inflamed surface, as their bite is irritating, but rather to the periphery. They should not be placed on conspicuous portions of the body, nor directly over a superficial artery, vein, or nerve. They are generally applied to the temples or the back of the neck in cerebral congestion or inflammation, in front of the tragus or to the mastoid in acute otitis media and acute mastoiditis, to the coccyx in congested or inflamed hemorrhoids, and to the perineum when the labia, scrotum, or penis are inflamed.

TECHNIQUE.—To avoid infection the site of the leeching should (if hairy, be first shaved) be washed with soap and water. The leech, in a pill-box, wine-glass, or test-tube, should be applied to the part and confined until it takes hold. Puncture of the skin or rubbing it with sweetened water or milk will favor the process. When the leech has taken hold it should not be disturbed until it drops off, which it will do when filled. Sprinkling salt over it, however, will cause it to let go. The application of hot fomentations will increase the amount of blood removed. When the leech drops off, bathe the bite with sterile water and apply a gauze dressing. If the bleeding continues and is troublesome, it may be controlled by compression, adrenalin solution (1:1000), alum, or tannic acid. If these fail excise the bite and suture the tissues.

Leeching followed by cupping is considered superior to venesection by the writer. Two groups of 3 or 4 leeches are applied, each group in a

liqueur glass, some distance apart on the lateral aspect of the thorax or abdomen. A flow of blood having thus been well established, the gorged leeches are removed, and the hemorrhage maintained or accelerated at will by applying cups alternately to the 2 groups of leech wounds. L. Plantier (Paris méd., Aug. 19, 1916).

The artificial leech consists of a small cupping apparatus and a scarifier. With this an ounce (30 c.c.) of blood may be withdrawn. W.

LEISHMANIOSIS. See KALA-AZAR.

LENTIGO.—DEFINITION.—Lentigo (ephelides; freckles) consists of yellowish, brownish, or blackish spots of pigment of the size of a pinhead or as large as a pea, occurring chiefly on the face and hands. Their gross appearance is familiar to everyone.

ETIOLOGY.—Freckles are usually due to the action of the chemical or actinic rays of the sun, although they may also be produced by exposure to arc light or to the X-rays. Congenital predisposition is believed by many to be necessary. They are more marked in persons of fair skin and in mulattoes, particularly in those having red hair and gray eyes. They generally appear during the summer and fade more or less completely during the winter. It is occasionally observed as one of the senile changes of the skin.

PATHOLOGY.—In freckles there is an increased deposit of pigment in circumscribed areas of cells in the basal layers of the epidermis.

TREATMENT.—An exfoliation of the epidermal cells containing the pigment is the object sought in treatment. **Mercury bichloride, acetic acid, sodium thiosulphate,** and similar preparations are used. Schamberg finds the following useful:—

℞ *Hydrargyri chloridi corrosivi* ... gr. iv-vj.
(0.26-0.4 Gm.).
Glycerini f3ij (7.5 c.c.).
Alcoholis,
Aquæ cologniensis,
Aquæ āā f3iiss (45 c.c.).—M. W.

LEPROSY.—DEFINITION.—Leprosy is a chronic infectious disease closely allied to tuberculosis, acquired by inoculation with Hansen's *Bacillus lepræ*.

VARIETIES.—It is customary to divide leprosy into two—sometimes three—general forms, the *tuberculous* and the *anesthetic*, the former being characterized by infiltration of the subcutaneous or submucous tissues and the formation of tubercle-like nodules; the latter by anesthetic areas denoting infiltration of the nervous supply.

SYMPTOMS.—The earliest symptoms of leprosy in the majority of cases, according to Morrow (who claims to have first called attention to the early evidences in the nasal mucous membrane) and other observers, are alteration of the voice, betrayed by a slight husky or rough phonation,—Besnier's *voix lèpreuse*,—which he likewise considers an early sign; rhinitis, with an abnormally free nasal secretion, sometimes epistaxis, and an increase in the salivary secretion.

Sticker noted that the nasal membrane could appear normal in the first stage or at most show a slight increase of secretion. The first visible change is a simple dry catarrh in circumscribed patches, which eventually present a raw surface. In advanced cases shallow or deep ulcers are visible in one or both sides of the septum. Sometimes there is only a hard swelling, which may extend to adjacent parts and produce stenosis.

In 1920 there were 242 cases in the United States, including: Louisiana, 87; California, 39; Texas, 33; New York, 28; Massachusetts, 13; Minnesota, 10; Florida, 7; Pennsylvania, 6; Connecticut, 5; New Jersey and Colorado, 3 each; Illinois, South Carolina and Wisconsin, 2 each. Philippines, 5500; Hawaii, 700; Canal Zone, 80; Porto Rico, 50. Hoffmann (Trans. Amer. Med. Assoc., Apr. 26, 1920).

Leprous lesions of the nasal fossa, the mouth, throat, and larynx were found by Jeanselme and Laurens in 60 per cent. of the cases examined.

The systemic invasion of leprosy is usually slow, years rather than months constituting the period of incubation. Occasionally, however, its onset is sud-

den and the disease progresses rapidly. The prodromal symptoms are mainly those of general neurasthenia: anorexia, chilliness, slight ephemeral fever, mental inaptitude, drowsiness, dyspepsia, vertigo, etc. These manifestations occur by exacerbations, and their recurrence is attended by more or less marked impairment of sensibility and other cutaneous functions, perspiration, etc., over restricted areas, fugitive erythema-like spots.

There is usually observed an essential leprous fever due to the presence of *Bacillus lepræ* or its toxins. This fever is always intermittent, if uncomplicated. It may occur at any period of the disease, including the so-called prodromal period of some writers, and may or may not be accompanied by an eruption. Since all forms of leprosy depend on the same organism, the fever probably occurs in all, although in varying degree. When fever of a continued type is observed, it is due to the presence of other toxins acting either with, or entirely apart from, those of *Bacillus lepræ*.

In the morning the pulse rate is higher than at evening, often markedly so. This condition is not due to the greater morning activity of the patient or to atmospheric changes. Honeij (Boston Med. and Surg. Jour., Feb. 12, 1914).

After the foregoing symptoms have shown themselves with varying activity at various times, receding as often with more or less rapidity and completeness, the erythematous spots become more persistent, are more highly colored and sensitive to the touch, and project beyond the surface to a greater degree. They are reddish brown, gray, dark yellow, or bronze, and of varying size from that of a dime to that of the palm. They may appear over any part of the body, the face, the trunk, and extensor portions of the limbs. After a time these spots also disappear, leaving a discolored patch, which in dark-skinned persons, such as the residents of South American countries, appear white as compared to their surroundings.

In some cases I had occasion to see in Mexico the appearance of the patients suggested the spots on leopard skins.

Tubercular Leprosy.—It is in this form, that most commonly observed, that the nasopharyngeal phenomena are the most marked.

The patient experiences slight difficulty in breathing through the nose, and the symptoms pertaining to the air tract already described become quite marked. Then comes the period during which the cutaneous lepromata of Leloir are formed.

Just as in tuberculosis the existence of a pretuberculous stage is sometimes recognized, there is in leprosy a stage of latency or preleprosis preceding the development of the more characteristic symptoms. Fever, intermittent, continuous, or irregular, and refractory to quinine, may be present years before the typical signs appear. Other early manifestations are weakness, lassitude, backache, dizziness, drowsiness, disturbances of the sweat function, precordial oppression, dryness of the nasal mucous membranes, and epistaxis. Barbézieux (Revue de méd., July, 1912).

Localized nodosities appear over various regions,—the face and hands particularly,—varying in size from small shot to a chestnut. The skin appears much thickened, hardened, and puckered, wrinkles being turned into deep furrows; the hairs are often changed in color and fall out. The projecting portions of the head—the nose, chin, and ears—taking part in the thickening, the face acquires a characteristic expression which fully accounts for the horror inspired by these wretched cases. The extremities, especially the hands and feet, are generally affected in the same way. Their skin being thickened and furrowed, they stand out stiffly and are used with difficulty.

The thickened areas, or "tubercles," do not all follow the same course. Some recede, leaving a depressed, more or less pigmented spot, while others proceed to ulceration. These ulcers are usually small, vary in depth, and their borders, as in the case of syphilis, are sharp-cut and have indurated edges. They heal and reappear several times in succession. When the ulcerative process invades the deeper tissues, they destroy them; mus-

cles, tendons, and even bone yield to its ravages; hence the mutilating effects of the disease. The mucous membranes of the mouth, tongue, pharynx, and larynx take part in the destructive process. The nasal bones and cartilages are markedly involved, the typical "saddle nose" indicating destruction of the supporting framework. A sniffing respiration indicates more or less obstruction to the respiration, by neoformations or depressed soft tissues.

Tubercular leprosy progresses slowly: eight to ten years, on an average. It is attended by eruptive and febrile exacerbations, each being followed by a period of comparative quiet. Gradually, however, the patient succumbs through invasion of the viscera, and death usually follows some intercurrent disease: pneumonia, pleurisy, etc.

Macular leprosy is described by some writers as a third type of the disease, and in a few cases the macules constitute practically the only symptom.

The character of the anesthesia depends on its location. In macules there is, as a rule, early loss of epicritic sensibility; in nodules and infiltrations the anesthesia is very variable; in a skin free of eruption a partial dissociation of the syringomyelic type is effected. These differences suggest the possibility that the cutaneous nerves may be involved in various ways. Not all the cutaneous lesions are anesthetic, 16 per cent. of infiltrations not being thus affected. Although absence of anesthesia, therefore, does not exclude leprosy, the touchstone in doubtful cases is its presence in some skin lesion or area. Anesthesia definitely improves under treatment by ethyl esters of the acids of chaulmoogra oil. J. N. Rodriguez (Philipp. Jour. of Sci., Aug., 1925).

Anesthetic Leprosy.—In this variety the spots are not as numerous, and often begin in the palms and soles. They resemble those in the tubercular form, being erythematous and hyperchromic. But disorders of sensibility are more marked from the start: hyperesthesia usually precedes anesthesia, and may be discerned not

only over the erythematous areas, but also over apparently healthy regions.

According to Dehio, leprosy skin-spots do not correspond to the distribution of the nerves, but may spread in all directions. Baelz observed that when the body of a leper was rubbed with a powder of fuchsin methyl violet, then covered closely with absorbent cotton, and pilocarpine was injected into the patient, the healthy perspiring skin became colored, whereas the leprosy non-perspiring spots did not.

The anesthesia is so marked that pin-pricks, burns, etc., are not felt. On the other hand, prickling and violent shooting pains are often complained of, certain nerves, particularly the ulnar and brachial, being sometimes greatly thickened and extremely sensitive to pressure. There is also exaggeration of the tendon reflexes. Paralysis of several muscles may occur, with all its attending complications. Considerable mutilation occurs in this form: the toes and fingers are destroyed, the loss being unattended by physical pain.

The general health gradually succumbs to the ravages of the disease, and, the viscera becoming involved, albuminuria, diarrhea, pneumonia, or some other intercurrent disorder ends the patient's suffering.

Complications of Both Forms.—Ocular affections of leprosy were studied by Panas. In the anesthetic form lagophthalmos, xerosis of the conjunctiva, iritis, cataract, and phthisis bulbi are frequent; in the tubercular varieties the cornea and conjunctiva are the chief seats of the lesion, though sometimes the iris, lens, and whole globe become implicated. The favorite seat is the corneoscleral border, proceeding thence into the corneal substance and to the deeper tissues.

Mental disorders are occasionally observed, melancholia especially. Inflammatory and diathetic disorders of the brain and spinal cord have also been noted as complications of leprosy.

Lepers, male and female, suffer from marked deterioration of the genital functions, and male lepers generally become impotent.

DIAGNOSIS.—The reported increase of leprosy in the United States to approxi-

mately 500 cases renders the recognition of the disease important.

In general, leprosy is always suggested by the dusky hue, the swollen skin, the overhanging eyebrows, and the raucous voice. The hands, too, have a thinned epidermis and an altered color which is different from that in any other disease. The presence of tubercles in the skin of the face, at the lips and about the nose, with others in the pendulous parts of the ears—all these should make a case suspicious. There are only two conditions which resemble tubercular leprosy, *viz.*, iodism and disseminated tuberculosis cutis. The first of these is seldom seen in the areas common to leprosy, and the nodules of iodism are highly inflammatory and ready to break down. With tuberculosis of the skin, the lesions are numerous, small, and deep-seated, under the epidermis as a rule; they are dirty white in color and seldom assume a reddened hue (Dyer and Hopkins).

Three laboratory methods of diagnosing leprosy: 1. Removal of a bit of tissue—even if it be only a macule or erythematous patch—and staining for the leprosy bacillus. 2. Examination of nasal mucus. Where the coryza usual in the leprosy is absent, 1 dram (4 Gm.) of potassium iodide should be given on two successive days to bring on secretion. Karinski's acid-fast bacillus, apt to be mistaken for Hansen's leprosy organism, can be distinguished from it by its ready growth on ordinary media and the fact that it is pathogenic to guinea-pigs upon intraperitoneal injection. 3. Intracutaneous injection of $\frac{1}{20}$ c.c. of Rost's leprolin, previously heated at 120° C. for twenty minutes. Leprolin is made by maceration of leprosy nodules and filtration, contains toxins, and was originally intended as a therapeutic agent analogous to tuberculin. In normal individuals, injection of leprolin causes a non-specific local reaction similar to that due to concentrated tuberculin. In the leprosy, on the other hand, there follows the formation of a small red nodule which in three days attains the size of a dime, with surrounding roseate area the size of a silver dollar. About the fourth

day there appears in its center a purplish spot, and later a small scale, which falls off on the twelfth to the fifteenth day. L. M. Pautrier (*Presse méd.*, Mar. 14, 1914).

Systematic examination of about 200 early and mild cases for leprosy bacilli in the nasal passages was carried out by the writer. A sterile swab was introduced into each nasal cavity and smears made and stained for acid-fast bacilli. In cases at first negative the procedure was repeated several times. Sometimes small pieces of tissue were also removed and examined in serial sections. Of the tubercular cases 77 per cent. gave positive nasal smears, of the anesthetic cases, 46 per cent., and mixed forms, 70 per cent. Many of the positive cases were holding occupations as porters, coachmen, bakers, candy venders, clerks, and students. J. C. Mukherji (*Medico-Surg. Jour. of the Tropics*, May, 1922).

Case of a Syrian, about 50 years old, who had come to America in 1900. The first symptoms dated from 1908. Admitting that the leprosy infection had been acquired in his home land, the minimal period of incubation must have been 7 years. In 1914 nodules were noted in the skin of the neck, head, arms, legs and on the tip of the tongue. Headache had been nearly constant since 1915, when indurated lumps began to appear on the forehead. The Wassermann was strongly positive. The diagnosis was advanced maculopapular and anesthetic leprosy. Acid-fast bacilli corresponding in morphology to *B. lepra* were demonstrated in the nasal secretion, cutaneous nodules and venous blood. D. C. Smith (*Va. Med. Monthly*, July, 1923).

The diseases from which leprosy particularly requires differentiation are syringomyelia, ainhum, tuberculosis, and syphilis. The similarity between leprosy and the two diseases first mentioned is such that they have been considered identical by some competent observers.

Syringomyelia.—In this disease Hansen's bacillus is absent. The frequent rise of temperature characterizing leprosy

does not attend syringomyelia. Though both diseases progress slowly, the active symptoms—headache, paresthesia, neuralgic pains—appear earlier in the former, while the dermal, muscular, vasomotor, and skeletal morbid changes do not appear in the regular order, as they do in syringomyelia. The hands and feet are first involved in leprosy; in syringomyelia the proximal parts of the limbs are first attacked and the destructive process is less marked than in leprosy.

Case of a woman 56 years of age who attracted considerable public attention on account of being a supposed leper. Further investigation, however, showed that the areas of erythema and the generalized anesthesia were a neurosis, due probably to locomotor ataxia, from which, upon investigation, she was found to be suffering. Troitskoia (Roussky Vrach, Aug. 11, 1912).

Ainhum.—Though Zambaco considers that etiologically ainhum and leprosy may be identical, their clinical aspects are sufficiently dissimilar to prevent errors in diagnosis. Ainhum occurs exclusively in negroes, and consists in the amputation of the little toe by an adventitious fibrous band. Hansen's bacillus has never yet been found in the diseased tissues.

Tuberculosis.—From this disease leprosy is differentiated mainly by the bacillus and through the absence in tuberculosis of anesthetic areas. The injection of tuberculin may, according to Babès and Kalindero, assist in the differentiation. In tuberculosis the general reaction, after the injection of tuberculin, begins about six hours after inoculation; in leprosy it generally comes on twenty-four or, less frequently, twelve hours after the injection of the tuberculin.

Syphilis.—The course of this disease usually serves to facilitate diagnosis, while Hansen's bacillus is not to be found. Fournier stated that general or local analgesia and anesthesia are frequently observed in syphilis; he found, however, that, if present at all, they occur on the dorsal surface of the metacarpal portion of the hand. The Wassermann reaction is frequently obtained in the tubercula. type of leprosy.

Carrying out 48 Wassermann reactions in leprosy, Montesanto and Sotiriadès found the reaction positive in 88.8 per cent. of the cases of tubercular leprosy; in the mixed form of leprosy it was positive in 75 per cent., while patients with anesthetic leprosy gave a positive reaction in 16.6 per cent.

The blood serum of 100 cases of undoubted leprosy in males was examined by the writer. Of this number 34 were nodular, 52 of the anesthetic, and 14 of the mixed form of leprosy. The positive Wassermann reactions for these several types were 17, 16 and 8, respectively, or 41 per cent. The author contends that the Wassermann reaction is characteristic of leprosy in these cases, even though not syphilitic. Iyengar (Indian Journal of Medical Research, Oct., 1919).

ETIOLOGY.—That leprosy is but slightly contagious is the opinion of the great majority of dermatologists. Not only have repeated inoculations failed to give rise to the disease, but cases have been reported showing that a person may reside with a leper, sleep and eat with him, nurse him, handle and wash his linen, and wear his clothes with impunity.

In spite of the general diffusion of the disease, those who know most about it doubt its contagiousness. In numerous mixed marriages coming under the personal observation of Zambaco the disease has never been transmitted from one party to the other. Often a single member of a family is a leper, and yet mingles without restraint with the others, adults and children. Nurses and attendants in leper hospitals, often religious devotees, care for lepers and live in their midst for years without contracting the disease.

An analysis by Chew of 1034 cases of leprosy in every stage of the disease showed that not a single case could be traced to contagion, such as sleeping with, eating with or nursing a leper, and handling or wearing his clothes.

Case in which an eruption appearing at the age of 7 years had been attributed to a recurrence of measles, and joint pains at 12 years and later had been regarded as recurrent rheumatic

fever. After the patient married, symptoms of tuberculosis appeared, with cutaneous nodules, from which the leprosy bacillus was cultivated. This patient's father had had mild leprosy and had died of intercurrent disease when the boy was 7 years old. The case is recorded as illustrating the contagiousness and prolonged latency of the disease, as well as its similarity to tuberculosis early in its course. P. Ramos Baez (Rev. de med. y cir., Apr. 10, 1925).

Still, there is considerable testimony in literature tending to prove that leprosy is contagious under certain circumstances, as will be shown under PROPHYLAXIS. Observers who have had occasion to study large numbers of cases generally uphold this opinion.

The history of the disease in all countries, and among every class of people, points to the certainty of contagion. It has been traced to sources. Its course has been progressive when segregation has not been enforced, and retrogressive when it has. In proportion to the failure to carry out segregation, the disease has advanced. Families which in England are and have been free from the taint of leprosy go to China, or elsewhere where leprosy prevails, and become leprosy. Dressers, nurses, and physicians in leper hospitals contract the disease quite frequently. To Louisiana the disease came with some French settlers; to New Brunswick with Frenchmen; to Minnesota with Norwegians, and so on. In each location where the disease develops carriers had come from leper-infected places. E. S. Goodhue (Med. Record, Jan. 27, 1900).

In the Hawaiian Islands kissing and nose-rubbing, which are the native forms of salutation; cohabitation, and the reception of the secretion of lepers through abrasions of the skin are considered as causes of communication. The natives eat *poi*, or *pa'ai*, as well as other kinds of food, with their fingers, from the same dish. Worse than this they make the native drink, called "*awa*,"

by masticating ti or ki leaves, and depositing the pulp into an earthen jar, where it is allowed to ferment, after which they drink it as an intoxicating beverage. The opinion generally prevails among physicians and the more intelligent classes of people on the island that leprosy is very frequently communicated by sexual intercourse. There is no reason why this should not be the case, as we know that abrasions of the mucous membrane are among the earlier manifestations of the disease. The mosquito, house-fly, and other insects have been accused of being carriers of the disease. C. E. Davis (Albany Med. Annals, Feb., 1901).

In a study of the histories of 10,000 cases in the Culi6n Leper Colony, the writer found that 29 per cent. of the lepers gave definite histories of contact with leper relatives. In only 1 per cent. had infection been transmitted through marriage. Denney (Jour. Amer. Med. Assoc., Dec. 29, 1917).

Clinical evidence tends to demonstrate that leprosy is not hereditary in the true sense of the word (though a fetus may be infected by a leprosy parent and be leprosy at birth), but that a proclivity to the disease is inherited by the offspring, and that exposure, in his case, will lead to its development.

In his investigation of 1034 lepers Chew noted that, of these, 10 were born leprosy; 21 contracted leprosy from their parents before puberty. The disease skipped the first generation to attack the second in some, and the third in others. There were 15 that were born leprosy of healthy parents.

Conditions capable of sufficiently reducing the vital resistance of the organism—insufficient or unwholesome food, excessive use of salt, a fish diet, exposure to cold and damp, alcoholism, malaria, overwork, syphilis, tuberculosis, etc.—are recognized predisposing factors.

According to Jeanselme and Laurens, and Sticker, lepers eliminate the bacillus of leprosy in enormous numbers through the upper respiratory tract and particularly the nasal cavities. During the active

stages of the disease the nasal secretions and the sputa of the subjects thus disseminate the bacillus of leprosy, by emptying their nostrils and expectorating over the restricted grounds in which they are segregated.

The telluric origin of leprosy would thus find an explanation. Though but slightly communicable by the leper himself when free, his compulsory segregation within a certain area of ground would thus cause him to transform this area into a focus of infection. His sputum, nasal secretion, and other contaminated ejecta would play the rôle that the sputum plays in tuberculosis.

A subject predisposed by heredity or debilitating factors could thus become infected in various ways by dust or water contaminated with secretions containing Hansen's bacilli. The upper respiratory tract is particularly exposed to infection through dust inhaled.

The breath of the patient, especially during the act of sneezing, has been found heavily charged with bacilli, and the air so charged may come into contact with the nasal mucous membrane of persons in the immediate vicinity.

Sticker found the bacillus in the nasal secretion in 83 per. cent. of patients. Lie examined 142 cases in this connection, including 50 with nodular leprosy and 92 with maculoanesthetic symptoms. The bacillus was discovered in 50 cases, 46 of the nodular type and 4 of the anesthetic.

Examining the nasal mucosæ of 250 children for leprosy bacilli, the writers found them in 35 instances; but in none of these were the nasal smears positive in the absence of positive skin lesions. Thus, nasal lesions appear to be altogether secondary manifestations in children. Not only is it a fact that the nasal mucosa is not often the site of the initial lesion in leprosy, but in young children it would seem that the initial lesion does not occur there at all. It may do so occasionally, however, in older individuals. F. Solis and H. W. Wade (*Jour. Philipp. Isl. Med. Assoc.*, Dec., 1925).

Abrasions and solutions of continuity of the skin or mucous membrane, etc., may thus also afford entrance to the germ.

The system is invaded by Hansen's bacillus through the skin or the mucous membrane of the nose, mouth and throat. The infection soon becomes generalized. The skin constitutes the optimum soil for the germ, and next is the lymphatic system; the liver, spleen and testes also form a favorable habitat. In any location, however, the germ lives in the connective tissue. It passes into the blood, but does not thrive there, except during exacerbations of the disease. A. Serra (*Gior. ital. d. mal. ven.*, Oct. 28, 1921).

On the basis of the histories of 259 lepers, the writers favor the view that the germ enters the body through abrasions or similar wounds of the integument of the exposed parts. The earliest recognizable lesion is in the anesthetic area. The more susceptible ages are in the first decades, although no age seems to be exempt. Callender and Bitterman (*Philipp. Jour. of Sci.*, May, 1925).

Morrow advanced the theory that, like syphilis, leprosy was usually communicated by sexual intercourse. In Chew's statistics but 7 cases out of 1034 can be traced to coitus; but, as already stated, the period of incubation of the leprosy is long and the disease may thus frequently be communicated and show signs of its existence long after intercourse. The bacillus has been found in semen.

Sex does not seem to have much influence upon the development of the disease, though male lepers are by far the more numerous. It may attack children as well as adults, but it is most frequently met with in persons between 20 and 45 years of age: the period of life attended by the greatest exposure.

The bedbug has been found to harbor the specific bacillus and capable of transmitting the disease in animals. It may prove to be one of the factors in the transmission of leprosy.

In a case reported by the writer, in which the infection was limited to a local focus, the disease appeared to have been transmitted by head lice. Fagerlund (*Finska l k. handl.*, July, 1925).

Leprosy found 14 times by the writer in an examination of 2780 rats. The pathological condition was much as observed by others, thickening of the skin, nodules in 1 case only, but ulcers in nearly every case containing enormous numbers of the acid-fast bacilli, morphologically identical with those of human leprosy. Agnes Walker (Jour. Amer. Med. Assoc., Oct. 3, 1908).

Having found acid-fast bacilli answering as far as our imperfect tests permit to the characteristics of lepra bacilli in a considerable proportion (about 30 per cent.) of specimens of *Acanthia lectularia*—a bedbug—up to sixteen days after feeding on lepers, this species of insect may constitute a very important agent in the spreading of leprosy. T. L. Sandes (Brit. Med. Jour., Sept. 2, 1911).

A total of 105 bedbugs fed on lepers, and 35 caught in the beds of lepers, and examined for leprosy bacilli, gave no evidence that these insects harbor or transmit the disease. Thomson (Brit. Med. Jour., Oct. 4, 1913).

Bedbugs can be induced to take up lepra bacilli with blood to which the bacilli have been added. Within the bugs the bacilli for a time increase in size and apparently in numbers; but they eventually disappear, partly by discharge with fecal matter, partly also by disintegration within the bedbugs. In the bugs thus infected the writers found the bacilli in the glands as well as in the alimentary canal. Bedbugs acquire lepra bacilli also with blood taken from human leprosy subjects, but not invariably. The bugs infected in the laboratory—presumably more heavily infected than those which are infected from human beings—were found capable of transmitting the bacilli by route of their sucking apparatus to the skin of animals bitten. Smith, Lynch and Rivas (Amer. Jour. Med. Sci., Nov., 1913).

Hansen's bacilli have been found in bedbugs and horse flies, while both the flea and mosquito have been accused of transmission on clinical evi-

dence. Evidences of direct contagion, on the other hand, are not convincing in comparison with the data which point to some sort of mediate contagion. In regard to hereditary transmission leprosy never descends as such, but abortion and bearing of inferior children are commonly observed in leprous women. Chabas (Chronica Medico-Quirurgica, July, 1918).

DISTRIBUTION.—Leprosy is most prevalent in India, where, according to Zambaco, there are 130,000 cases; but the disease is thought to be increasing. It is also met with extensively in China; but less so in Persia, Japan, Tonquin, Siam, Anam, the Antilles, and South America.

Plumacher estimates that there are 30,000 lepers in the departments of Boyaca and Santander, in Colombia.

Leprosy also exists in Norway, Sweden, Russia, Spain, Italy, Roumania, Greece, Turkey (at least 4000), and in a modified and light form in France.

In the English-speaking sections of North America the cases are comparatively few. There are 5 foci, 2 in Canada, aggregating about 40 cases, and 3 in the United States, aggregating about 300 cases. Sporadic cases are occasionally met with in our cities.

Leprosy distribution in the United States studied through a letter of inquiry addressed to every state health officer. The establishment of the Federal leprosarium in Carville, La., in 1921, was of distinct value, harboring as it has 297 cases from all parts of the country. Of this number, however, 39 escaped, 36 died and 12 were discharged. In various states cases of leprosy still occur pending their removal to the leprosarium: California, 20; Louisiana, 13; Arizona, 5; Minnesota, 4; Illinois, 4; Pennsylvania, 2; North Dakota, 2; and each of the following, 1: Colorado, New York, Maryland, Nevada, Montana, Arkansas, Alabama, Utah and New Jersey. Maine is doubtful owing to the presence of a small leper colony in New Brunswick, while in Texas "several" of 11 lepers are reported to have been sent to the leprosarium. F. L. Hoff-

mann (Jour. Amer. Med. Assoc., Nov. 22, 1924).

PATHOGENESIS.—A specific bacillus closely allied to the bacillus of tuberculosis has been shown by Hansen in 1871 to be the exciting cause of leprosy. The labors of Neisser have confirmed Hansen's discovery. *Bacillus lepræ* is a long and slender, motionless rod, with slightly tapering ends. It reacts in the same way that the tubercle bacillus does to coloring reagents, but much more readily—a distinctive feature—and takes aniline dyes, which tubercle bacilli do not. Again, the bacilli of leprosy are usually much more numerous.

The researches of the last twelve years have only more firmly established the lepra bacillus of Hansen as the specific cause of leprosy. During the last decade numerous attempts have been made to cultivate the bacillus, but no medium has been discovered on which it will invariably grow. It has not been proved that the bacillus is present and can lead a saprophytic existence on decayed organic matter, such as decomposed fish, meat, rice, or in the soil. J. M. H. Macleod (Brit. Jour. of Dermat., Oct., 1909).

The results of animal experiments demonstrate the fact that direct communication of the disease may take place from individual to individual without the presence of the bed-bug or other parasites as intermediate hosts. In the examination of blood from patients suffering from leprosy the serum has been shown to contain specific antibodies of different kinds against certain constituents of *Bacillus lepræ*. In addition to the presence of specific bodies, they have demonstrated that complement is present in normal quantities. Agglutinins are present, though not in very large amounts. The opsonic content is probably affected at different stages of the disease. Duval and Gurd (Arch. of Intern. Med., Feb., 1911).

The acid-fast bacillus known in the human leprosy lesion as the Hansen organism can be cultivated *in vitro*

under special nutritive conditions. The initial multiplication away from the tissues of the host occurs in the presence of the split products of animal protein, the amino acids, and under no other conditions. Duval and Harris (Jour. Med. Research, May, 1913).

Arning thought he had successfully inoculated a condemned criminal with matter obtained directly from a leper, but the subject was subsequently found to belong to a family (including his son and nephew) in which the disease existed: a fact demonstrating his proclivity to the disease. More recently, however, leprosy has been produced in the monkey.

The writer succeeded in producing leprosy in the monkey (*Macacus rhesus*). Four injections at intervals were followed by the formation of hard, nodular masses that slowly increased in size, and the skin about which showed numerous small, indurated areas. On rupturing, one of the masses discharged a grumous material, which, on microscopic examination, was found to contain large numbers of leproid cells filled with acid-fast bacilli. Cultures prepared from this material remained sterile with respect to pyogenic microorganisms; however, *Bacillus lepræ* was recovered in pure culture upon special artificial media.

Forty-six days after the first injection the monkey showed typical signs of disseminated infection, and presented the clinical picture of human leprosy of the tuberculous type of the disease. C. W. Duval (Univ. of Penna. Med. Bull., Feb., 1911).

Occurrence of leprosy in a monkey in which the disease developed thirteen months after the first, and nine months after the last, injection of a pure culture of *Bacillus lepræ*, the infection being identical in symptom-complex with that in man, and terminating fatally. Duval and Couret (Jour. of Exper. Med., Mar., 1912).

The introduction of the virus through abrasions, scarification with medicinal

substances, and vaccination, which together represented almost one-fourth of the etiological factors noted by Chew in his 1034 cases, demonstrates that transmission by inoculation is, in reality, an important pathogenic factor.

The bacilli are to be found in all the tissues and liquids of the diseased areas only, and particularly in the lepromata.

At autopsy in a case of extensive leprosy, the liver and spleen were found crowded with the bacilli, while there were relatively few in the kidneys, lungs and bone marrow. None were detected in the brain or spinal cord. Whereas, in acute tuberculosis, there is clearly an elimination of tubercle bacilli in the bile, in this leprosy case there were no bacilli in the bile, the organisms being retained by the macrophage cells of the Kupffer type. Sabrazès (C. r. Soc. de biol., Dec. 18, 1925).

The blood of lepers in various stages of the disease was carefully studied by Winiarski. When leprosy has not given rise to great changes in the organism, the composition of the blood is not much altered. No change in its composition in the various forms of leprosy (anesthetic, nodose, and mixed) could be demonstrated. In chronic cases the number of blood-corpuscles was always found to be diminished, on an average, 17.9 per cent. in men and 12.3 per cent. in women. The hemoglobin was decreased, on an average, 6.3 per cent. in men and 2.4 per cent. in women. The white blood-corpuscles were usually normal in number. In all cases of leprosy a large preponderance of polynuclear leucocytes was noted.

A high globulin content of the serum in active cases has been reported. The bacillus is readily found.

According to Rabinowitsch, lepra bacilli circulating in the mother's blood can be transmitted to the fetus in utero through the blood channels.

Bacillus lepræ is easily found in the blood in cases of leprosy. The method consists in collecting 0.1 to 1 c.c. of the patient's blood from the tip of the finger or toe (free from lepra lesions), or from a vein, in about 5 to 20 c.c. of

a 2 per cent. solution of acetic acid, in which the erythrocytes are dissolved. The mixture is centrifugated for about fifteen minutes and the sediment examined for alcohol acid-fast bacilli.

The method of staining used is one usually followed in the examination for tubercle bacilli; the sediment is spread on a slide, dried, fixed, stained with carbol-fuchsin, decolorized with 30 per cent. hydrochloric acid solution in 95 per cent. alcohol, and counter-stained with methylene blue. Damaso Rivas (N. Y. Med. Jour., Jan. 25, 1913).

That segregation is an effective prophylactic measure for the protection of the public at large against leprosy is undoubted. The same statement would be applicable, however, were syphilitic, tuberculous, and other infectious subjects to be compulsorily isolated and ostracized from society. Indeed, it would apply more forcibly, since leprosy is one of the least contagious of the infectious diseases, though undeniably so in individuals who are pre-disposed to it.

The bacilli of leprosy are only found in diseased tissues and in the blood, discharges, etc., of the latter. It is a question, therefore, whether the healthy areas of skin and mucous membrane are not subject to reinfection from external cause (see ETIOLOGY) capable of inducing the disease in any pre-disposed subject.

The leprosy bacilli multiply in the lymph channels, where they acquire their pabula, and are set free in the lymph spaces by softening of the area in which they are imbedded. The infection spreads from the skin to the deeper tissues, the osseous and muscular lesions being due to cicatricial pressure upon the nerve trunks. The cutaneous and nerve lesions are thus linked pathologically. E. Muir (Indian Jour. of Med. Res., July, 1923).

Segregation within a restricted district under such circumstances would greatly compromise the chances of recovery of the sufferers so segregated. Constantly exposed to contaminated soil and surroundings, reinfection would seal the doom

of many who, under the influence of hygienic surroundings, would be restored to health by appropriate treatment. Lazarettos, pest-houses, etc., would thus become foci of infection.

This is strongly sustained by the fact that in such institutions practically all the patients die of the disease or its complications, while, among lepers only exposed to the average contaminating influences of cities, many are saved.

Of 1034 cases of leprosy observed during a period of fourteen years and nine months by Chew, 422 were cured, while medicines failed to make any lasting impression on the remaining 612.

According to Morrow's computation, the number of lepers in the Molokai settlement (Hawaii) averaged, at the time, about 1200, but he contends that, notwithstanding the optimistic view of the health authorities that leprosy is on the decrease, the annual consignment of lepers to the settlement shows but little, if any, diminution. "All the indications point to the existence of a vast deal of latent leprosy, which, as the disease develops into a recognizable form, must continue for many years to come to furnish a constantly recurring series for the leper colony."

What probably does exist in Hawaii is a large number of vulnerable individuals, vulnerable through the operation of the various factors enumerated, and especially active, perhaps, in these islands on account of the deteriorated state of the natives. These etiological factors, as well as susceptible subjects, are to be found in all countries and especially in districts where poverty, filth, bad food, and alcoholism prevail. Were compulsory isolation abandoned, therefore, leprosy—like syphilis, tuberculosis, cancer, etc.—would assume the position of a general disease, its development being commensurate with its low degree of contagiousness and the hygienic level and customs of the communities exposed. In the United States the debilitating influence of excessive and unduly prolonged physical and mental activity would tend to increase vulnerability, and the dissemination of leprosy might thus be greatly enhanced.

Segregation of lepers is, therefore, im-

perative, but only on the condition that they be compensated for their isolation on behalf of others by adequate protection against continued infection and by the most conscientious efforts to restore them to health and to their families.

In some "settlements," "lazarettos," or "pest-houses" these unfortunate patients (some of which may not be leprosy and be suffering from tuberculosis, syringomyelia, or syphilis) are practically assimilated to criminals awaiting the death penalty, while neglect, both general and professional, is insidiously acting as executioner.

Such neglect on the part of municipalities—such wretchedness—is not compatible with modern civilization. Sanitary regulations to protect communities involving the sequestration of innocent sufferers should not destroy with one hand to save with the other. All should come in for their share of the benefits, if equity is to prevail and if the cruelties of the dark ages are not to be perpetuated. Consumptives, inebriates, the insane, etc., enjoy all the advantages of well-appointed and comfortable sanatoria; so should the leper receive his share of all that human compassion can afford to relieve him of physical sufferings and of the mental torture that ostracism entails.

A sanatorium for lepers should, in the light of our present knowledge, and in keeping with settlements under United States authorities, be conducted much on the same lines as one for consumptives: scrupulous cleanliness, pure air and sunlight, *strict attention to the destruction by fire or antiseptics of all substances containing bacilli*, especially the secretions of the mouth and nose and the discharges originating from tuberculous nodules. With abundant wholesome food, comfortable surroundings, distraction, and constant professional care, the lives of these victims could be made bearable; the fetters which sanitary rulings impose upon them would hardly be felt, and many would be returned to their homes.

As to the immigration of lepers into the country, Dr. Bracken, of Minneapolis, basing his opinion upon a study of the Minnesota colony, suggests that the family history of all immigrants from a country

where leprosy prevails should be secured before they are allowed to embark for America, no member of a leprous family being permitted to land upon our shores. This procedure would doubtless prove effective were it properly carried out.

The conception of leprosy as a progressive and inevitably fatal disease is not necessarily founded on fact. G. H. Taylor has pointed out that thickening and tenderness of the peroneal nerves and slight anesthesia of the parts supplied are not uncommon in individuals showing healed leprous lesions *post mortem*. E. Muir, moreover, has demonstrated leprosy bacilli in many persons who do not manifest leprous lesions, and in others who appear to recover spontaneously. Editorial (Lancet, Sept. 19, 1925).

TREATMENT.—Attention to the nasal cavities, the mouth, and throat is of primary importance. As a detergent, a solution of 1 dram (4 Gm.) of common salt in 1 pint (500 c.c.) of water is suitable. As a wash, the following mixture can also be confidently recommended after extensive trial in disorders of the upper respiratory tract:—

℞ *Borate of sodium*,
Bicarbonate of sodium of each ʒss (2 Gm.).
Fluidextract of
Canadian pine ... fʒj (4 c.c.).
Glycerin fʒij (8 c.c.).
Water Oj (500 c.c.).—M.

This may be used night and morning with an atomizer producing a coarse spray, the cavities being thoroughly drenched. In large colonies under municipal management **borax** and **bicarbonate of sodium**, equal parts, may be procured in bulk and dealt out to patients with instructions to use 1 teaspoonful of the powder to a pint of lukewarm water. An economical way is to inhale the solution from the hand, using the latter as scoop. When ulceration is present, the local treatment for syphilitic rhinitis (*q.v.*) is indicated. The **secretions**, as already stated, **should be destroyed**, and the use of **spit-cups** rigidly enforced.

Segregation where lepers have previously lived without resorting to such precautions should be avoided.

Cleanliness of the surface should be carried to the maximum possibility compatible with the patient's strength. As a curative measure, Baelz, of Tokio, recommended 3 to 5 strong **mineral baths** at 45° to 53° C. a day for a period of about one month. His results were excellent. **Sea-bathing** was extensively used, and with marked advantage, during the early part of the century. At first warm **sea-water baths** were given, until all "scaly incrustations" were removed; after this "a cure was soon obtained, especially in young persons, by bathing in the open sea."

To enhance the resistance of the patients, in the Philippines, the writer employed a **high calory diet**, an adequate supply of fresh vegetables and fruits, and, to supplement the insufficient fish ration with a cheap available protein, he used mungo, *Phaseolus aureus* Roxburgh, a bean which is abundant in the islands and contains about 22 per cent. of protein. The conclusion seemed justified that this high calory diet, with an adequate supply of mineral matter, of vitamins and of that substance found in green vegetables which aids in the deposition of calcium, is beneficial to lepers and that their weight and general health are improved thereby. Embrey (Philipp. Jour. of Sci., Apr., 1923).

Among the internal remedies recommended, **chaulmoogra oil** and its derivatives hold the first place. The oil has been administered in doses of from 5 to 200 drops. By beginning with small doses and gradually increasing the quantity given, the gastric disorders occasionally following its use may generally be avoided or at least retarded until active benefit is procured. It is borne more easily by lepers than by healthy subjects, and its use can be continued years, if need be. Many cases have been reported in which permanent cure had been obtained.

If given by mouth, **chaulmoogra oil** should be administered in doses of about 6 drops daily, or less often if progress can thereby be obtained. The use of **magnesium salts** as laxatives and of **calcium salts** as adjuvants to the oil treatment seems to be indicated.

B. E. Read (China Med. Jour., July, 1925).

The genuine chaulmoogra oil is expressed from the seeds of *Taraktagenos kursii*, but a number of closely related species of *Hydnocarpus* yield oils of similar composition, which are regarded as of almost equal value in the making of preparations to be used in leprosy.

For intramuscular injection the **chaulmoogra ethyl esters** are considered preferable to the oil, being more rapidly absorbed, although the active substances occurring in the body after absorption appear to be the same with the 2 preparations.

As described by G. A. Perkins, of the Culion Leper Colony, Philippine Islands, the ethyl esters are prepared by mixing 5 liters of alcohol with 100 c.c. of sulphuric acid and 10 liters of chaulmoogra oil, and boiling the mixture vigorously for 48 hours. The product is subjected to various processes for purification and is sterilized and sealed in bottles.

Reduction of the local irritation upon injection has been found to result from addition of $\frac{1}{2}$ per cent. of iodine to the ethyl esters. The esters are first distilled and steamed, freed of water by heating to 150° C., and the iodine stirred in while hot. A final heating to 160° C. for 1 hour effects changes in the manner of combination with iodine which result in a less irritating product and which are marked by a change in color from green to reddish brown. The iodine apparently combines with some highly unsaturated constituents of the ethyl esters.

Mixtures of the ethyl esters with 10 per cent. of creosote and with both $\frac{1}{2}$ per cent. of iodine and 10 per cent of creosote have also been prepared and used.

The so-called **Mercado mixture** is prepared as follows: About 2 liters of olive oil, U. S. P., are heated to 120° C. and 400 Gm. of resorcinol, U. S. P., and 550 Gm. of camphor, U. S. P., are dissolved in it. Sufficient olive oil is then added to make 6 liters, and the product mixed with 6 liters of refined chaulmoogra oil of not over 6 per cent. acidity (as oleic acid), and sterilized in small bottles by heating to 150° C. The original Mercado formula also called for 250 c.c. of ether. This can be added later before use. According to Perkins, the ab-

sorbability of Mercado mixture is not very different from that of the ethyl esters, volume for volume, but the esters have the advantage of double the concentration of the former.

As a standard treatment the writers use weekly injections of mixed **ethyl esters** of the acids of **chaulmoogra oil** with 2 per cent. of iodine in chemical combination. The amount used starts at 1 c.c. (16 minims) and is gradually increased to a maximum of 4 or 5 c.c. (1 or 1 $\frac{1}{4}$ drams) for adults. Three times each day, 1 $\frac{1}{2}$ hours after meals, the patient receives capsules containing the fatty acids of chaulmoogra oil with 2 $\frac{1}{2}$ per cent. of iodine chemically combined. The dosage for the first 15 days is $\frac{1}{2}$ Gm. (3 grains) per 100 pounds of body weight 3 times daily; for the second half of the first month, $\frac{1}{2}$ Gm. (5 grains) per 100 pounds; for the first half of the second month, $\frac{2}{3}$ Gm. (10 grains) per 100 pounds; and after that, 1 Gm. (15 grains) per 100 pounds of body weight. This means, for example, that a 150-pound man would get 1 $\frac{1}{2}$ Gm. (23 grains) per dose or 4 $\frac{1}{2}$ Gm. (68 grains) per day. It is probable that the oral administration of chaulmoogra oil derivatives is of minor importance compared with the injections.

In treating leprosy, it is important to make use of all auxiliary agencies to build up and maintain bodily vigor. Hypodermic injections of the **ethyl esters** into leprous nodules are followed by marked swelling with ultimate recession of the lesions. This is a valuable auxiliary treatment for especially resistant lesions.

The results of the **chaulmoogra oil** treatment thus far have been so satisfactory that lepers come willingly for treatment.

Following a course of treatment extending over about a year, 48 lepers, treated according to the new method, were paroled in October, 1919. McDonald and Dean (Public Health Reports, Aug. 20, 1920).

In 21 lepers at the San Francisco Hospital, the **ethyl esters of the total**

fatty acids of chaulmoogra oil were injected intragluteally at weekly intervals, the dosage varying according to the patient's weight and reactions. **Butyl and propyl esters** were later found to cause less pain and were substituted in the later treatment of the cases. In the few early cases treated, the remedy was of great value, but in advanced cases the results were not marked. The injections must be kept up at least 3 years and much longer in the advanced ones; it is possible that many of these will be cured after years of treatment. H. Morrow, E. L. Walker and H. E. Miller (Jour. Amer. Med. Assoc., Aug. 5, 1922).

Trying various procedures, the writer obtained best results with **intravenous injections of crude chaulmoogra oil**, 5 to 10 minims (0.3 to 0.6 c.c.) at body temperature, 1 to 3 times daily, with a fortnight's rest after 4 weeks' injections. He also found effective the intravenous and oral use of **sodium hydnocarpate**, which is, however, expensive. General measures comprise: **Abundant food**, with plenty of **milk**; a literally **open-air life**; gentle **exercises** and daily **baths**; **happiness of mind**, obtained by kindly personal interest, amusement, and remunerative work. P. Harper (Brit. Med. Jour., July 8, 1922).

The results of treatment at Culion Leper Colony in the Philippines were as follows: By Sept. 30, 1923, 4067 patients had received antileprotic treatment; of these 55.9 per cent. were improved, in 36 per cent. the condition remained stationary, 6.4 per cent. were worse, and 1.7 per cent. had died. Cases classified as improved and stationary should be considered together, for without treatment the disease would have progressed in most instances. In 30 per cent. of the cases plain **chaulmoogra ethyl esters** were given, and in 65 per cent. these esters were administered with **2 per cent. iodine**; the improvement was about the same for both. Of 44 cases treated with plain **morrhucic ethyl esters**, 34 per cent. showed improvement; 45 per cent. of 80 patients receiving the

iodized drug improved. The improvement rate was higher in females than in males. Young people up to 20 seemed increasingly amenable to treatment as they approached maturity, but from 20 to 30 (height of sexual activity) the improvement fell off. The next decade was one of greater improvement for both sexes, but in the 5th decade, the women, disturbed by the menopause, showed a marked drop. Time and regularity of treatment are important factors. Improvement seemed to be affected by total dose, and not by size of dose as compared to tolerance of the individual. This points to the need of some preparation that can be given in larger doses with less reaction, such reactions being distinctly injurious. H. W. Wade (Jour. Philipp. Isl. Med. Assoc., Sept.-Oct., 1923).

Of several treatments used at San Lazaro, the **ethyl esters of chaulmoogra oil** with $\frac{1}{2}$ per cent. of **iodine** yielded the best and most rapid results with the least local and constitutional reactions. In addition to the intramuscular injections, small doses (averaging 5 drops) were also given by the mouth. Gavino and Tietze (Jour. Philipp. Isl. Med. Assoc., Feb., 1925).

Purified forms of chaulmoogra oil or its esters, such as **antileprol**, are available. **Antileprol** is given in doses ranging from 5 to 50 drops in milk or capsules.

Chaulmoogra oil became official in U. S. P. X (1926) as *Oleum chaulmoograe*, and is described officially as a yellow or brownish-yellow liquid, or, below about 25° C., a whitish soft solid. It has a characteristic odor and somewhat acrid taste. It is sparingly soluble in alcohol, soluble in ether and chloroform. Dose, 15 minims (1 c.c.).

Æthylis chaulmoograe, U. S. P., consists of the ethyl esters of the fatty acids of the oil, and is a clear, pale yellow liquid with a slight fruity odor, insoluble in water but miscible with alcohol, ether and chloroform. Dose, by mouth or intramuscularly, 15 minims (1 c.c.).

The fractionation of chaulmoogra oil yields, according to Sir Leonard Rogers (Brit. Med. Jour., Oct. 21, 1916), several

different portions, that of the lowest melting point yielding fatty acids, the sodium salts of which are readily soluble in water, and only moderately irritant. The sodium salt, **sodium gynocardate**, which forms the greatest proportion of those present, may be given intravenously to man in leprosy in the form of a 2 or 3 per cent. solution to which $\frac{1}{2}$ per cent. **phenol** has been added, sterilizing in an autoclave. Doses of 6 to 50 mgm. ($\frac{1}{10}$ to $\frac{9}{10}$ grain) have been given to man without any toxic effects, although there often follows a definite local reaction and sometimes fever. In thoroughly treated cases there was very marked improvement, with healing and disappearance of local lesions; disappearance of the bacilli from open lesions; return of sensation in anesthetic areas, and restoration of function in paralyzed parts. Such results are not obtained from its subcutaneous use.

Sir Leonard Rogers (Lancet, June 4, 1921) also tested the action of other oils with a large content of unsaturated fatty acids, *viz.*, **codliver oil**, **linseed oil**, **Japanese sardine oil**, and **soya bean oil**, and found the codliver preparation, **sodium morrhuate**, the most effective, given intramuscularly or intravenously. He reported good results even in advanced cases, and advised shifting from 1 oil to another when benefit from any 1 ceases.

Nastin, a bacterial fat obtained from a streptothrix isolated from leprosy nodules, has been praised. The best results seldom exceed marked improvement.

Of 6 cases treated by **nastin** which had a duration of from five to sixteen years, 5 greatly improved, and 1 was practically cured. **Nastin** has in suitable cases the power of destroying the leprosy bacilli which are present in the organism, and so ameliorating the symptoms, or even curing the lesions of leprosy. Max Rudolph (Arch. Brasileiros de Med., vol. ii, No. 3, 1913).

Vaccine therapy, the agent mainly used being **leprosin**, a bacterial product of the leprosy bacillus, seems worthy of trial.

Twenty-two patients treated with **vaccine**, 5 of whom have practically recovered and 15 have shown marked

improvement, while the remaining 2 patients showed neither improvement nor increase. Improvement is very slow. The anesthetic patients should be given much larger doses of vaccine than the tubercular ones. Rost (Indian Med. Gaz., July, 1912).

The writer reports marked improvement in 2 cases of leprosy in which he injected **antianthrax vaccine**. He concludes from the results obtained that antibodies fatal to the lepra bacilli were produced, specimens from the nasal discharges previously found to contain active bacilli having been found sterile after the injections. Campos (Vida Nueva, Havana, Sept., 1918).

Ichthyol was strongly recommended by Unna, who gave about 10 grains (0.6 Gm.) of it a day in divided doses. According to De Brun, **ichthyol**, beginning with 30 to 45 grains (2 to 3 Gm.) a day, and reaching $2\frac{1}{2}$ drams (10 Gm.) a day in a short time, gives rise to no unpleasant by-effects, and proves effective in the tubercular form of leprosy.

Ichthyol soap or the pure drug may also be employed locally. **Pyrogallie acid** and **chrysarobin** have likewise been recommended by Unna.

Crocker administers **corrosive sublimate** hypodermically. A hypodermic syringe of a solution varying in strength according to age is injected into the buttocks once a week. **Euophen**, **thyroid substance**, and **salicylic acid** may also be mentioned among the remedies meriting a trial.

Good results from **iodalbin** internally in 20 grain (1.25 Gm.) doses, together with **iodinized autogenous serum**, serum from bullæ made by applying carbon dioxide snow to leprosy skin lesions being withdrawn and re-injected. Wayson (Arch. of Dermat. and Syph., Mar., 1921).

According to Wildish, **antimony** in the form of **tartar emetic** intravenously, or "**oscol stibium**" intramuscularly (2.5 to 6 c.c. daily), or **colloidal antimony**, has decided value, especially in advanced cases with paralysis and ulcers.

Colloidal antimony, 1 to 3 c.c. (16 to 48 minims) intramuscularly, given with marked results in 4 cases. Cawston

(Jour. of Trop. Med. and Hyg., Feb. 1, 1922).

Arsphenamin has been tried, but it does not seem to influence materially either form of leprosy.

In cases where the patient is not too weakened from the disease **arsphenamin** may be administered without harm. Some improvement may be expected especially in early cases. Creighton Wellman (N. Y. Med. Jour., Nov. 16, 1912).

Eucalyptus was advocated in leprosy by Hollman, who for 2 years used it with considerable success both internally and by means of **baths**. Of 275 cases treated, all were improved, the skin becoming softer and more pliable, the facies more normal, and the neuritic pains less; the abscesses of the skin and mucosæ healed, and the fever decreased.

The writer reports 3 cases in which the use of **guaiacol**, both internally and externally, gave good results. Internally it was given in the form of pills, each containing 0.1 Gm. (1½ grains) of **guaiacol**, 0.04 Gm. (¾ grain) of **eucalyptol**, and extract of licorice. The dose was 2 pills morning and evening, gradually increased until 10 pills were being taken daily. Externally the **guaiacol** was applied with a brush, and sometimes covered with a dressing of gauze and cotton. A **generous diet** is to be combined with this treatment, and an **alkaline bath** given twice a week. N. Maldaresco (Semaine méd., Jan. 18, 1911).

Tubercular nodules may be destroyed by **galvanocautery** or **thermocautery** followed by local **antiseptic lotions**. If this procedure is objected to, their absorption may sometimes be obtained by local applications of **iodine** or **mercurial ointment**.

The most effective method of dealing with the ulcerations met with in tubercular leprosy is to scrape them and then apply a wash of 5 per cent. **benzoyl chloride** in petrolatum. Wise and Minett (Jour. of Trop. Med. and Hyg., Sept. 2, 1912).

In the large number of incipient cases where the disease is localized

(peripheral or neural) any treatment that will remove the circumscribed area or focus of infection, without opening up channels for metastatic dissemination, will effect a cure in from six to twelve months time. The initial focus may remain localized for a time extending from a few months to years, or even a lifetime. E. S. Goodhue (Amer. Med., Mar., 1913).

Freezing the lesions of tubercular leprosy with **carbon dioxide snow** liquefies the resistant covering of the lepra bacilli. The frozen leproma disappears after a time, leaving a soft pigmented area surrounded by a pigmented areola. Untreated lepromas also disappear at the same time, leaving soft, slightly pigmented spots. The lepra organisms are found in these spots as fine granules, rarely as bacilli. A. Paldrock (Arch. f. Derm. u. Syph., Apr. 14, 1923).

The **X-rays** have given some encouraging results, and should be used before the internal lesions of the disease have developed to any marked degree.

C. E. DE M. S.

LEPTANDRA.—*Leptandra* (veronica; Culver's root) is the rhizome and root of *Veronica virginica*, a plant of the family Scrophulariaceæ. It contains a bitter principle known as leptandrin, as well as saponin, tannin, resin, starch, etc. Leptandrin as sold is an impure resin or alcoholic extract.

PREPARATIONS AND DOSE.—*Leptandra*, N. F. (leptandra). Dose, 15 grains (1 Gm.).

Extractum leptandræ, N. F. (extract of leptandra). Dose, 4 grains (0.25 Gm.).

Fluidextractum leptandræ, N. F. (fluidextract of leptandra). Dose, 15 minims (1 c.c.).

PHYSIOLOGICAL ACTION.—*Leptandra* is classed among the drastic cathartics, though its action is mild and slow as compared with that of colocynth and jalap. Like several other cathartics, leptandra has been credited with cholagogue properties.

THERAPEUTICS.—In indigestion with deficient secretion and constipation, lep-

tandra is useful, combined with podophyllum or with aromatics. When stools are clay-colored, showing a deficiency of bile, this agent will, according to some, bring about bilious discharges, even when there is diarrhea. The extract of leptandra is an eligible form for administration in small doses where merely a laxative action is desired. The root of leptandra should be dried for clinical use, when fresh its action is too violent. W. and S.

LEUCINURIA AND TYROSINURIA.

Leucin ($C_6H_{13}NO_2$) and tyrosin ($C_9H_{11}NO_3$), related decomposition-products of proteids, usually occur together in the urine and in the organism itself. When retrograde tissue changes are rapid, as in extensive suppuration and gangrene, they form in large amounts and pass into the urine, largely supplementing urea. They also occur in the urine in acute atrophy of the liver, acute phosphorus poisoning, and at times in leukemia, typhoid fever, and variola. Leucin is normally present in the liver, pancreas, spleen, lymph glands, salivary glands, and thyroid and thymus glands.

Detection of Leucin.—*Microscopical examination* of a urinary sediment containing leucin will reveal it in the form of yellowish, highly refractile spheres, resembling oil-globules. When pure it crystallizes in scales or rosettes, often of irregular shapes, and has a greasy feel. It is insoluble in ether, thus differentiating it from oil-globules and in mineral acids; it is partly soluble in water and alcohol, and completely in caustic alkalies. Chemical tests are confirmatory if enough leucin is available.

Hoffmeister's Test.—Heating the solution with mercury protonitrate yields a deposit of metallic mercury.

Scherer's Test.—When evaporated with nitric acid on platinum-foil leucin leaves a colorless residue which, if heated with potassium hydroxide, forms drops of an oil-like fluid which does not adhere to the platinum.

Sublimation Test.—Leucin heated in a glass tube open at both ends to about $348^{\circ} F.$ ($170^{\circ} C.$) sublimes in feathery particles. Further heat fuses it, and causes it mostly to disappear.

Separation Test.—Evaporate the urine, and dissolve the residue in boiling alcohol. When cooled the leucin will be deposited in whitish plates or masses. S.

LEUCODERMA.—DEFINITION.

—Leucoderma (vitiligo; achromia cutis; acquired leucoderma; acquired piebald skin; pigment atrophy) is an affection characterized by variously sized and shaped whitish patches, usually surrounded by abnormally pigmented borders.

SYMPTOMS.—This disease appears as rounded, oval or irregular, milk-white or pinkish-white spots which spread more or less rapidly, coalescing at times to form large patches. These patches are smooth, soft, sharply defined and level with the surrounding skin surface, which latter is the seat of increased pigmentation, usually brownish yellow in color. The hairs in the affected area may turn white, especially if the patch extends into the hairy scalp. When exposed to the sun, especially during the summer, the pigmentation around the patches is augmented, thereby increasing the disfigurement. Slowly progressing, the disease becomes conspicuous after a few years. The greater part of, or, indeed, the whole, body may become involved. Leucoderma generally persists during life. The favorite seat of the disease is the back of the hands, the neck, face, and the trunk. Subjective symptoms are absent.

DIAGNOSIS.—Leucoderma must be differentiated from chloasma, tinea versicolor, morphea, and leprosy. In chloasma the patches are brownish yellow; there are no white spots. In tinea versicolor the patches are brownish yellow, covered by furfuraceous scales; this is caused by a fungus. In morphea there is a thickening of the patch at first, which is followed by atrophy. In leprosy the patches may be whitish or yellowish, but the surface is anesthetic.

PROGNOSIS.—The disease is practically incurable, although in a few rare cases spontaneous recovery has occurred.

TREATMENT.—Though the treatment is highly unsatisfactory, a cure has been reported from the use of **thyroid extract**. Duhring advised small doses of **arsenic**, long continued. Lotions of **mercury bi-**

chloride or of acetic acid may be applied. The ultra-violet rays seem useful. W.

LEUCORRHEA. See VAGINA AND VULVA, DISEASES OF.

LEUKEMIA AND PSEUDO-LEUKEMIA, OR HODGKIN'S DISEASE.

LEUKEMIA, OR LEUCOCYTHEMIA.

DEFINITION.—A disease of the hematopoietic system, usually chronic, insidious in onset, and characterized by a very great increase in the number of the leucocytes, with marked alteration of the leucocytic formula. There are two types—the myeloid and the lymphoid.

MYELOID LEUKEMIA.

SYMPTOMS.—The onset is insidious and it is probable that by the time symptoms attract the attention of the patient the disease is far advanced. In practically all cases in which the blood was examined at the time the patient first came under observation the picture revealed was that of a fully developed leukemia. A physician is first consulted, as a rule, because of pain in the left upper quadrant of the abdomen in association with a mass, which on examination is found to be the spleen. Less commonly, severe nosebleed or hemorrhage from some other part of the body is the first evidence of the disease. In most cases, however, if a careful history is elicited it will be found that for weeks or months, or perhaps longer, the patient may have experienced a vague sense of ill health with later loss of appetite, an increasing tendency to fatigue, and loss of weight. These symptoms may remain stationary or abate, only to recur.

As the disease progresses, dyspnea

becomes troublesome, even before marked anemia occurs, and is due to the crowding of leucocytes in the capillaries of the lungs. In the terminal stage of the disease anemia becomes marked, giving rise to pallor, vertigo, headache, and edema of dependent parts. Dyspnea increases.

Fever is present in every case. It is irregular in type and for a time may be absent. The temperature is usually under 102° F. (38.9° C.). Preceding death there may be either a rise or fall in temperature. Tenderness on pressure or even pain may be felt by the patient over the sternum and the shafts of the long bones. Hemorrhage is common later in the disease. It may be slight or severe and may occur from any of the mucous membranes, or into various organs, including the brain. The amount of blood lost may be lethal.

Early in the disease slight or moderate enlargement of the spleen may be the only abnormality detected. Later the spleen becomes huge and may extend into the pelvis. It is usually firm, smooth, and not movable. The normal contour is preserved and the notch or notches may be readily felt. Sometimes pain on pressure is elicited, and auscultation may reveal a friction synchronous with the respiratory movements of the diaphragm. Variations in the size of the spleen may occur during the course of the disease. After hemorrhage or during the course of an intercurrent infection marked diminution may be observed. Hemorrhage into the spleen may cause a sudden enlargement.

The liver is almost always increased in size, extending 1 to 4 fingers' breadth below the costal margin, or even below the transverse umbilical

line. It is smooth, firm, and regular in outline. Usually it is not painful and only occasionally is tenderness complained of on pressure.

The heart may be displaced by upward pressure of the enlarged spleen. The muscular element of the first sound is diminished and a soft systolic murmur at the apex may be heard.

Usually, the second sound at the pulmonic cartilage is accentuated. Percussion over the chest posteriorly may reveal dullness due to compression of the base of one or both lungs. Unilateral or bilateral pleural effusion may be found, and when unilateral it is most commonly present on the left side.

The peripheral lymphatic glands are rarely enlarged.

Uric acid is present in the urine in a larger amount than is the case in any other disease. It is derived from the nuclei of the disintegrated leucocytes. Very interesting and suggestive is the fact that muscle and joint pains are usually absent, notwithstanding the very large amount of uric acid found in the urine. Albumin may or may not be present. It may appear irregularly during the course of the disease, particularly during febrile periods. Casts, usually of the hyaline variety, may be found from time to time.

Blood.—The characteristic changes consist in the great increase in leucocytes and the appearance in large number of myelocytes, the latter being the distinguishing feature of the myeloid type of leukemia. The leucocytes usually number from 100,000 to 500,000 per c.mm.; less commonly more than 1,000,000 white cells per c.mm. are counted. The ratio between leucocytes and erythrocytes,

instead of the normal 1:500, is usually 1:10. Later, as the number of leucocytes increases and erythrocytes decrease, the ratio may be 1:1. Cases have been reported in which the leucocytes exceeded the erythrocytes in number.

Report of 2 cases of myeloid leukemia setting in at the ages of 2 weeks and 8 months. The former of these cases ran the longer course on account of X-ray treatment, dying at 20 months. The latter was acutely fatal. Malmberg (*Acta Ped.*, July 1, 1925).

A very marked alteration occurs in the leucocytic formula. The polymorphonuclear cells make up about 30 to 60 per cent.; small lymphocytes about 1 to 5 per cent.; large lymphocytes 3 to 30 per cent.; eosinophiles 1 per cent.; myelocytes 30 to 50 per cent. All the leucocytes normally found in the blood are much increased in actual numbers, a fact often overlooked in a study of the percentages. Very occasionally the small lymphocytes are reported absent. Early in the case the erythrocytes are but slightly diminished; later they may be reduced to 1,000,000 per c.mm. Nucleated red cells are very common, even with an erythrocyte count of 4,000,000 or more per c.mm. As a rule, the hemoglobin is reduced, percentages of 50 or less being quite common. (See colored plate opposite page 380, Vol. V.)

The writers found that a protease is present in the lymphocytes of chronic lymphoid leukemia and in the leucocytes of acute and chronic myeloid leukemia and of pus. Lipase occurs in the white cells in the same conditions. Amylase is contained in the granular leucocytes of pus and of myeloid leukemia, acute and chronic, and in the lymphocytes of chronic lymphoid leukemia. Maltase

is likewise a product or constituent of these cells. Morris and Boggs (*Archives of Intern. Med.*, Dec., 1911).

The writers cultivated leucocytes from leukemic blood, according to

In myeloid leukemia the platelets may be normal, enormously increased, or greatly diminished. Hemorrhages may occur when they are much increased. In lymphoid and acute leukemias, they are generally below nor-



Case of chronic lymphatic leukemia, showing outline of liver and spleen below costal margin. (*H. K. Thoms.*) (*Yale Medical Journal.*)

Carrel's method. They found that young leucocytes were capable of energetic multiplication, and by further development might be transformed into giant cells and microphages. Avroroff and Timofeerosky (*Roussky Vrach*, May 11, 1913).

mal, and petechiæ may attend such decrease. Minot and Buckman (*Amer. Jour. Med. Sci.*, Apr., 1925).

LYMPHOID LEUKEMIA.—This is less common than the myeloid leukemia. The onset is insidious, the

first complaints being malaise, weakness, loss of appetite, and pallor. The lymphatic glands enlarge early in the course of the disease, and in some cases this is the first evidence of abnormality. The enlargements may be noticeable for years before symptoms attract the attention of the patient. All the lymphatic glands of the body enlarge. Externally, the cervical, axillary, and inguinal glands become the largest, while internally the

pains in her bones from time to time, particularly the breast bone, and also in the small of her back and ribs. Otherwise she had not had any illness which appeared to bear on her present condition.

The nodules first appeared on the lower part of the abdomen, and rapidly spread over the front of the body. Each individual nodule was at first small, about the size of a pea, and grew in the course of a few days to the size of a large raisin. When the nodules first ap-



Leukemic nodular infiltration of the skin. (Rolleston and Fox.)
(British Journal of Dermatology.)

mediastinal and abdominal glands attain great size. Usually there is little or no pain in the glands.

Dyspnea, cough, and edema of the arms or legs are often very troublesome and are due to pressure. Itching of the skin may cause great distress, frequently being associated with urticaria. Lymphomata may occur in the skin over any part of the body.

Case of atypical myeloid leukemia with nodular infiltration of the skin. The patient, a widow aged 58 years, complained of "lumps in the skin," which she had first noticed two months previously. For several months before this she had noticed

peared they were much darker than at present, in fact almost black; they did not cause any itching or pain. She was fairly well in herself, only rather weak. She had lost about 16 pounds in weight in the last two months. H. D. Rolleston and W. Fox (Brit. Jour. of Dermat., Dec., 1909).

Fever is present in most cases, and nausea and vomiting are common. Anemia occurs earlier than in the myeloid type and when severe causes edema, breathlessness, tinnitus aurium, vertigo, and headache. Hemorrhages are more common than in myeloid leukemia.

The lymphatic glands are movable, hard, discrete, as a rule not tender, and rarely attain the size seen in Hodgkin's disease. The liver and spleen are enlarged in all cases, but to a lesser extent than in the myeloid form.

Examination reveals a large amount of uric acid; albumin and hyaline casts are commonly found.

The number of leucocytes per c.mm. varies between 10,000 and 1,000,000, the average number being about 100,000. It is often impossible to make a diagnosis from a leucocyte count alone. A differential count, however, always establishes the diagnosis. The lymphocytes vary from 80 per cent. to 100 per cent., both the large and the small varieties partaking in the increase. The polymorphonuclear cells are reduced in number and eosinophiles and mast cells are often absent. Myelocytes may or may not be present. Even early in the course of the disease but 2,000,000 or 3,000,000 erythrocytes per c.mm. may be found, and as the disease progresses their number is still further reduced. The hemoglobin percentage is low. Normoblasts and megaloblasts are usually present and poikilocytosis is common. The erythrocytes stain poorly.

Nodular Leukemias.—This term has been applied to cases in which nodules or tumors of a leukemic type are found. Such cases have been reported under a great variety of names, *e.g.*, chloroma, Mikulicz's disease, Kaposi's disease, mycosis fungoides, sarcomatosis, etc. (As a matter of fact, there may be present in leukemias, not only nodules or tumors, but also pigmentation, edema, vesicles, macules, papules, diffuse erythroderma, urticaria or pruritus).

Chloroma, as described by Pearson, is a rapidly growing and very destructive new growth, usually occurring in the young, some or all of the tumor masses having a

greenish color. The growths are most commonly found in or on the bones of the skull, chiefly in the orbital or temporal regions, and may be associated with exophthalmos, tenderness over the affected bones, nerve impairments due to pressure, anemia and cachexia with fever, and a hemorrhagic diathesis. Histologically it may be divided into the myeloid and the lymphatic types. The clinical course closely resembles that of acute leukemia. The green color may also sometimes be seen in the leucocyte layer of centrifugated blood. The tumors may behave like malignant neoplasms in invading the adjacent bones.

The blood picture in chloroma is similar to or identical with that of myeloid or lymphatic leukemia, especially the acute forms of the latter. The total number of leucocytes is, of course, usually increased, but it may occasionally be normal. Late in the disease the leucocyte count falls, descending below the normal. In lymphatic chloroma, when the leucocytes are low in number, the lymphocytes are large and atypical. In myeloid chloroma there are numerous myeloblasts, myelocytes, and nucleated redds. Chloromatous tumor cells have been found in the blood stream.

Myeloma is differentiated from chloroma by hyperplasia in the bone marrow and the absence of leukemic blood findings; chloroma may show characteristically situated tumors and greenish urine. *Hodgkin's disease* shows a grouped glandular enlargement, polymorphonuclear leucocytosis, eosinophilia, and pruritus. In *lymphosarcomatosis* the process begins in one group of lymph-glands, while in chloroma there may be general lymphatic involvement.

In the treatment of chloroma, the measures used in the ordinary leukemias may be tried. The X-rays have yielded improvement in some instances. The prognosis, however, is unfavorable, death usually taking place within a few months.

Mikulicz's disease is characterized by symmetrical enlargement of the lachrymal and salivary glands. These glands are hard but painless. The enlargement has been ascribed to their content of lymphoid tissue. At times evidences of deficient endocrin functioning exist. Local complications comprise rhinitis, conjunctivitis, retinitis, papillitis, choroiditis, lymphoma of the orbit, and

dacryoadenitis. Typically, the process eventually spreads to all of the lymphatic ganglia and the spleen. The blood picture suggests lymphoid leukemia.

Some improvement has resulted from **arsphenamin** and **mercury biniodide**. Other useful agents are the **X-ray**, **radium**, and **benzol**. **Argyrol** may be used for the conjunctivitis, and disturbances of the puncta and tear-ducts may call for appropriate treatment.

ACUTE LEUKEMIA.—This is rarer than the chronic form and is most often encountered in children. Females seem to be more frequently attacked than males. Because of its resemblance to an acute infection, it is probable that in some cases a correct diagnosis is not made. Indeed, the diagnosis depends almost solely on the blood examination.

Pain in various parts of the body and weakness are the first symptoms. Weakness increases rapidly and in a short time the patient is prostrated. Hemorrhage is extremely common and occurs from the nose, gums, tonsils, gastrointestinal mucous membranes, and into the skin. Cerebral and retinal hemorrhages may occur. In some cases severe bleeding has been the first symptom. Frequently ulceration occurs at the site of hemorrhage, especially in the mouth, where it simulates noma.

Acute myeloid leukemia is frequently accompanied by cutaneous, mucous, or visceral hemorrhages. In certain cases these hemorrhages are so abundant or numerous that an actual hemorrhagic form of myeloid leukemia can be spoken of; the author reports 6 cases of this kind. Ter-Barseguian (*Revue méd. de la Suisse Romande*, Aug., 1913).

Fever is usually present and may be high (103° to 104° F.—39.5° to 40° C.). The temperature curve is very irregular and may suggest sep-

sis. Occasionally it resembles the curve of typhoid fever.

Just before death the temperature may become subnormal. The skin takes on a wax-like yellowish or grayish pallor and puffiness of the face and edema of the ankles are commonly observed. Toward the end dyspnea may occur, the pulse increases in rate and becomes feeble. The liver, spleen, and lymph-glands enlarge rapidly. The cervical and submaxillary nodes are often the first to show enlargement. Sometimes the course of the disease is so rapid that death ensues before the glands enlarge. Albumin may appear in the urine; casts are usually absent. Hematuria may occur. The excretion of a large amount of uric acid is very common.

Pathognomonic evidence of the nature of the disease is to be found in the blood, examination of which reveals a great increase in the number of leucocytes. Usually the proportion of white cells to erythrocytes is 1 : 20 or 1 : 10. Cases are reported with ratios of 1 : 3 and 1 : 2. The actual number of leucocytes per c.mm. of blood ranges between 200,000 and 500,000. In the majority of cases there is a great increase in the number of lymphocytes (80 to 100 per cent.), the large cells predominating. The polymorphonuclear cells constitute but a small percentage. Eosinophiles and myelocytes are usually less than 1 per cent. Rarely the myelocytes predominate. The erythrocytes number about 3,000,000 per c.mm., though occasionally they may fall as low as 1,000,000. A few nucleated red cells are usually observed. The hemoglobin is reduced to less than 50 per cent. in most cases.

In the acute types of the disease, as noted by Schultze, the process goes on so rapidly

that young types of cells, the lymphoblast and the myeloblast, invade the blood. These cells look so much alike that it is impossible to distinguish them except by a test, which depends on the fact that all myeloid cells possess ferments in their protoplasm, while lymphatic cells are free from such ferment. The blood-smear is fixed in formalin, then dipped for a short time in a 1 per cent. aqueous solution of alphanaphthol, then for a short time in a 1 per cent. aqueous solution of dimethylparaphenylenediamine (Merck). A deep-blue color will form in the presence of ferments; hence only cells derived from the bone-marrow will exhibit blue granules.

The occurrence of a positive *indophenoloxidase reaction* in large non-granular cells in acute leukemia is certain proof of their myeloid nature, and allows a diagnosis of acute myeloid leukemia to be readily made from blood examination. Cases of acute myeloid leukemia may occur, however, in which the type of blood formation is so embryonic that the oxidase reaction is valueless for differential diagnosis, but even in such cases the histological characters of the large leucocytes may render a diagnosis possible. J. S. Dunn (Quarterly Jour. of Med., Apr., 1913).

An acute benign form of leukemia is discussed by the writer. He describes it as an acute febrile disease, usually with a local infectious, but non-suppurative, process, with enlargement of the lymphatic glands of the neck, axillas, or groins, or combinations of these, enlargement of the spleen, a relative mononucleosis, with or without moderate leucocytosis (usually less than 20,000), and the presence of lymphoblasts. The condition occurs mostly in young adults and is distinguishable from true acute leukemia only in that the patients recover. J. G. Cross (Minn. Med., Oct., 1922).

Case of acute lymphatic leukemia in which the course was so rapid that the patient, aged 42, was dead before he realized he was ill. A small sore on the lower lip had nearly healed in 3 days, at which time he noticed bruises on the chest and had headache. When

seen, there were 8 bruises of varying size on the chest, legs and arms, and a few petechiæ, including 3 in the mouth. The man's color was particularly good. No enlarged glands or organs could be found. Blood coagulation seemed normal. He protested against going to bed, stating that, aside from headache, he felt perfectly well. Next day he had "a fit," and was found comatose, with unequal pupils, death following some hours later, evidently from extensive meningeal hemorrhage. D. Hall (Pract., June, 1925).

In the writer's case of acute lymphatic leukemia the lymphocyte count reached 320,000. The course was fulminating, with bleeding from the gums, intestines and nose, into the skin, and finally into the meninges. The oral mucous membrane was gangrenous. Violent nervous manifestations developed, followed by coma and death. Cate (China Med. Jour., Jan., 1926).

The disease usually runs its course in a few weeks or months, death occurring from progressive inanition. Hemorrhage and rupture of the spleen sometimes cause a fatal termination. An infection may occur as a complication and cause death from sepsis.

DIAGNOSIS.—If the blood is examined the diagnosis of leukemia is made with great ease, whereas without such an examination it is often impossible to make a correct diagnosis. Acute leukemia presents the greatest difficulty in diagnosis. The fever, if accompanied by intestinal hemorrhage, suggests typhoid fever. Cases that present spongy, bleeding gums, with hemorrhage into the skin, suggest purpura hemorrhagica. Many cases strongly resemble sepsis. As previously stated, however, an examination of the blood, including a differential leucocyte count, will clear away the difficulties in diagnosis. It should be borne in mind that occasionally, in chronic lymphoid leukemia, the leuco-

cytes may be no more numerous than is frequently the case in infections; also in the chronic myeloid, as well as in the lymphoid type, the leucocytes may be reduced to normal numbers during an intercurrent infection. Therefore, it is essential to make a differential leucocyte count to avoid mistakes in diagnosis.

Leukanemia.—This term was originally applied by Leube in 1900 to a disturbance characterized, as described by Symmers, by an extremely rapid course and by changes in the blood, bone marrow, spleen, liver, and lymph-nodes partaking both of the nature of pernicious anemia and myeloid leukemia. It is probably not an independent disease, but one of a group of rapidly progressive derangements of the blood-forming tissues, due to infection. The provocative agent seems to strike the bone marrow with such intensity as to cause the appearance of both types of cells, erythroblastic and leukocytic, in the circulating blood.

ETIOLOGY.—Practically nothing is known concerning the cause of leukemia. Cases have been reported following trauma, but up to the present time no definite evidence has been produced to show that injury bears a causal relationship to the disease. Malaria and other infections, poor food, insanitary conditions, worry, overwork, and heredity are of little importance etiologically.

It has been suggested that leukemia, particularly in the case of the acute type, is infectious in origin, and various bacteria and bodies thought to be animal parasites have been reported as present in the blood of some of these patients.

Some acute infectious disease is the forerunner of leukemia and allied conditions. Acute leukemia is in itself the clinical picture of an acute infectious disease or intoxication. Many of its manifestations resemble those of severe diphtheria and

other septic diseases. Hansemann (Berl. klin. Woch., Jan. 5, 1914).

The frequent coincidence of leukemia and tuberculosis; the predominant or even exclusive localization of the tuberculosis in the hematopoietic organs in leukemia, and the localized tuberculous infection of the glands in the beginning of leukemia, as observed in some cases by the writer, suggest that leukemia may be induced by tuberculous infection. Weil, Isch-Wall and Pollet (Bull. Soc. méd. des hôp. de Paris, Feb. 6, 1925).

A man who had been hit in the chest by a log showed progressive weakness for 3 weeks, followed by bleeding from the gums. Changes pointing to myeloid leukemia were found in the blood, and death took place 1 month after the trauma. Reference made to 5 other cases of fatal acute leukemia following trauma. Martinelli (Polyclin., Sept. 7, 1925).

Fatal case of myeloid leukemia in a technician who had been engaged for several years in preparing radioactive substances of the thorium group. In another technician fatal pernicious anemia was induced. Apparently, radiations as well as infections may induce changes in the hematopoietic cells, the nature of these changes depending on individual predisposition. Fatal leukemia occurred in a woman who had received a single intensive 7-hour X-ray exposure 7 years before. P. Emile-Weil (Presse méd., Sept. 30, 1925).

Rigid investigation has failed to prove definitely the claims of bacterial or parasitic causations. Some authorities consider the chronic lymphatic type of leukemia to be closely related to the neoplasm known as lymphosarcoma.

Myelogenous leukemia is a malignant neoplastic disease. Its onset is insidious, and it is usually fatal. It is sometimes favorably influenced by the appearance of an intercurrent disease. In many of the organs there are masses of cells identical with those of bone-marrow, which are foreign

to the organs involved, and are apparently metastases. Harris (Amer. Jour. Med. Sci., July, 1908).

Acute myeloid leukemia in 2 previously healthy children with apparently mild scarlet fever developed varicella during convalescence and in connection with this a severe hemorrhagic sepsis, fatal in a week. The necropsy findings were those of acute myeloid leukemia. Animals inoculated with cultures from the 2 children confirmed the diagnosis of a streptococcus sepsis. C. Sternberg (Wiener klin. Woch., Nov. 23, 1911).

Case of lymphoblastic leukemia in a child 5½ years old, noteworthy because the lymph-glands of the neck and elbow were converted into a common heterotopic growing tumor which produced macroscopically the picture of Sternberg's leucosarcomatosis. Herxheimer (Münch. med. Woch., Nov. 18, 1913).

Leukemia is a rare disease. The myeloid form is seen more frequently than the lymphoid. Most cases of chronic leukemia occur between the ages of 20 and 50 years. It is almost twice as common in males as in females. On the other hand, acute leukemia is more often observed in females under the age of 20 years.

The average duration of the chronic form is only fifteen months from the time of first observation. Death may occur by the failure of the erythroblastic function of the bone-marrow, and the presence of severe anemia with large numbers of nucleated red cells is of grave prognosis. Exhaustion of the leucoblastic tissues, as shown by the decreased production of the leucocytes and the immaturity of the forms produced, would seem, however, to be the more usual cause of death. Treatment by X-rays and arsenic causes no improvement or a striking one which is only temporary. The fatal issue sometimes is hastened by these measures of treatment. The

absence of marked splenic enlargement in the acute cases is suggestive of a failure of the protective action of the spleen. Panton and Tidy (Lancet, May 18, 1912).

PATHOLOGY.—The essential lesions are found in the spleen, bone-marrow, and lymph-glands.

The *spleen* is always enlarged and, in the chronic myelogenous form, may reach huge proportions. The organ retains its shape, is smooth, hard, and circumscribed areas of perisplenitis are visible. Adhesions may bind the spleen to the surrounding structures. On section the color is mottled gray or grayish red. Hemorrhage into the substance may be found. Microscopically, the structure closely resembles bone-marrow. The Malpighian follicles disappear and are replaced by masses of leucocytes through which capillaries course. The masses of leucocytes are composed of myelocytes, polymorphonuclear neutrophils, and mononuclear cells. Many nucleated erythrocytes are present.

Seven cases of leukemia developing after an accident involving the spleen, including 2 in which it followed splenectomy. Amputation of the thigh was responsible for the leukemia in Murrich's case. In both the writer's cases the spleen was directly injured in a fall or in an accident, bending the body far over backward. The extreme pallor and weakness and the leukemic blood-findings continued a progressive course until each of the young men died of intercurrent pneumonia in about two months after the traumatism. Facchini (Gaz. degli Osped., May 18, 1913).

Changes in the *bone-marrow* are observed chiefly in the shafts of the long bones and in the sternum. The fat is replaced by soft, rather tough tissue, described by Sir William Osler

as resembling the consistent matter which forms the core of an abscess. It is grayish white in color, but takes on a reddish tint on exposure to the air. Microscopically the mass is composed of myelocytes, polymorphonuclear neutrophiles, eosinophiles, mononuclear leucocytes, and erythrocytes.

The *lymph-glands* in the myeloid form are slightly, if at all, enlarged, though in the abdomen they may reach the size of a walnut. In the lymphoid form considerable enlargement of the glands of the entire body may occur. Many of the glands show a normal microscopic picture, while in others changes similar to those in the spleen and bone-marrow occur. The lymphatic tissue in the gastrointestinal tract may be involved and ulceration of Peyer's patches is sometimes found.

The *liver* is enlarged in most cases. It is grayish yellow in color. Microscopically, the capillaries are found overdistended with leucocytes, causing pressure atrophy of the liver cells. Numbers of distended capillaries may coalesce, thus forming leucocytic masses sometimes called leukemic tumors.

The *lungs* show changes like those described in the liver, *i.e.*, overdistention of the capillaries by leucocytes. This encroaches upon the air space and is one of the causes of dyspnea. Compression of the bases of the lower lobes from pressure of the enlarged liver and spleen is commonly found. An effusion of serum is not uncommonly present in one or both pleural cavities. Marked edema of the lungs may be found.

The *heart* chambers are usually distended by clotted blood. Ecchymoses

of the pericardium and endocardium are often found. Microscopically the picture of fatty degeneration is presented.

The *thymus gland* may be slightly enlarged, though, as a rule, no changes are found.

The capillaries of the *kidneys* may be overdistended with leucocytes and, just as in the liver and lungs, they may coalesce to form leukemic tumors. The same coalescence may occur in the capillaries of the skin.

The *tonsils* are often enlarged, especially in the acute cases, and ulceration may be present here and also in the nasal and pharyngeal mucous membrane. The gums are often spongy and ulcerated. No changes are found in the nervous system, except those secondary to hemorrhage into the brain.

PROGNOSIS.—Leukemia is probably always a fatal disease. There is no well-authenticated instance of recovery on record. In acute cases death occurs in a few weeks or months. With the chronic form patients may live for one to five years. Osler placed on record, however, the fact that he had had occasion to observe a patient with chronic lymphatic leukemia ten years after the diagnosis had been made. Remissions in symptoms occur once or more during the course of the disease. Leukemic individuals are especially prone to infections, boils and abscesses being of frequent occurrence. Death from septicemia is not uncommon. Tuberculosis, especially the miliary form, is very common. It has been frequently observed that during the course of an infection, *i.e.*, pneumonia, carbuncle, erysipelas, the leucocytes may be diminished near or to normal num-

bers. The number of leucocytes per c.mm. of blood is not always in direct relationship to the severity of the symptoms, though, as a rule, the greater the number, the more severe the disease. In acute lymphoid leukemia a preponderance of large mononuclear cells usually indicates an earlier fatal termination.

TREATMENT.—There is no curative treatment for leukemia. Among drugs, **arsenic** is given first place. It should be used to the point of tolerance, if used at all.

Better results have lately been obtained by the use of **Röntgen rays** and the internal administration of **benzol**. The former has been tried over a longer period than the latter, and in the hands of experts it is possible in almost every case to reduce the number of leucocytes to normal and at the same time to cause the general symptoms to vanish. The rapidity of reduction in the number of leucocytes depends on the intensity of treatment. The differential leucocyte count approximates normal. Early in the treatment of myeloid leukemia the pathological cells decrease and may even disappear, while in the lymphoid type the qualitative change is observed only after the number of leucocytes has been reduced to or near normal. The erythrocytes and hemoglobin are increased, after a preliminary decrease, in almost all cases of myeloid leukemia, and less frequently in the lymphoid variety. As the number of erythrocytes is increased the nucleated red cells decrease. The spleen slowly decreases in size and may even return to normal. The first evidence of beneficial action of the rays on the spleen is a diminution in the resistance on palpation, and coincidentally

the patient is conscious of a sense of diminished weight in the abdomen. As the shrinking of the spleen progresses pain may occur, due to stretching and pulling on the adhesions which attach the organs to surrounding structures. Enlarged lymphatic glands disappear rather promptly. The excretion of uric acid is increased, fever disappears, strength returns, and the patient is enabled to assume an occupation. The best results are obtained in chronic myeloid leukemia.

In the beginning of treatment, especially, if it is intensive, dizziness, vertigo, vomiting, diarrhea, and loss of weight may occur. These symptoms are those of a toxemia, due to a sudden liberation into the circulation of a large quantity of the destructive products of leucocytes, and their appearance demands either a diminution in the intensity or the suspension of treatment for a time.

The good results of Röntgen-ray treatment are brought about by: (a) The primary destruction of lymphoid and myeloid tissue with inhibition of their ability to proliferate; (b) diminution of toxin formation due to inhibition of the formation of pathological cells; (c) the occurrence in the blood of a substance formed from the decomposition products of destroyed leucocytes which influence the blood-making organs.

In the course of treatment of chronic leukemia by the rays, four phases are observable, viz.: (1) The initial disturbance of the general well-being; increase in leucocytes with a secondary, step-like decrease; (2) gradual betterment in the general condition and gradual increase in the erythrocytes and hemoglobin; (3) a period

of latency, during which the patient may feel practically well; (4) a recurrence of symptoms.

Radium is also used with benefit, and according to some, is the best therapeutic agent available.

In 8 cases of myeloid leukemia treated by **radium exposures of the spleen**, an apparent cure was noted at first, followed by recurrence in 2 to 18 months. To postpone and attenuate recurrences, the treatment should be as intense as possible, with longer intervals. The bone-marrow may also be treated. The writers are confident that survival for 5 or 6 years can be procured by well ordered radium and X-ray treatment. Rénon and Degrais (Bull. de l'Acad. de méd., Feb. 15, 1921).

The author prefers the **X-rays**, because of the limited area of effective action of radium. He has seen but 2 cases in which their use was not followed by marked improvement. H. B. Thompson (Amer. Jour. of Roentgenol., Nov., 1921).

The **X-rays** and **radium** are often used in combination by the writer, who applies radium over the spleen and the X-rays over the osseous and glandular structures. Enough radium must be used to secure deep effects. Soiland (Jour. of Radiol., Dec., 1921).

Myeloid case in a boy of 14 in which, upon relapse after discontinuance of radium treatment for 2 months, 2 further applications were followed by a rapid leucopenia and anemia resulting in death. Caution in regulating radium dosage is enjoined. Whitcher (Boston Med. and Surg. Jour., Sept. 7, 1922).

Radium is so efficient in *splenic leukemia* that in no other fatal disease can it be said to be more efficient. A single treatment suffices in some instances to bring about marked improvement within 24 hours, with restoration of appetite and sleep. The spleen recedes, usually to the rib margin, and the blood count drops so rapidly that the applications have to be stopped temporarily. In *lymphatic leukemia* and the mixed leukemias,

the scattered enlarged nodes render impracticable the application of the radium rays in sufficient dosage to obtain as active results as in splenic anemia. Even then the enlarged glands return to normal in some cases and the white cell count is greatly reduced. Aikins (Amer. Jour. of Roentgenol., Nov., 1923).

Irradiation tried out in 80 cases of chronic lymphatic leukemia and 57 cases of the acute form, **radium** or **X-rays** being used, while 30 untreated cases served as a control group. While the duration of the disease was not influenced in either form of the disease, the symptoms in the chronic form, and particularly in chronic myelogenous leukemia, were undoubtedly benefited. Improvement was obtained in 47 per cent. of 61 cases, slight improvement in 30 per cent., and none in 23 per cent. In 10 per cent. the patient's efficiency was strikingly increased. Minot and Isaacs (Boston Med. and Surg. Jour., July 3, 1924).

Case of normal pregnancy and labor in a patient who had had myeloid leukemia at least 18 months. **Radium** treatment had been given 15 months before the parturition. A year later both the woman and child were still well. Chiari and Dautwitz (Wien. Arch. f. inn. Med., Nov. 1, 1925).

The duration of the period of latency averages about six months, at the end of which time another course of treatment is necessary, as indicated by a return of abnormal cells to the blood in increasing numbers. The patient may thus sometimes be carried through a number of years before radiation becomes ineffective. Sometimes after a short period of latency an "explosive" recurrence ends in death. The duration of the other phases is also variable.

Conclusions reached that under proper dosage almost hopeless cases will respond rapidly to **X-ray** treatment; that this improvement is marked enough to cause the patients to feel that

they are practically cured; that after cessation of treatment the disease recurs; and finally, that these recurrences are also amenable to treatment, though the response is successively less satisfactory. Thomas (Cleveland Med. Jour., Apr., 1912).

The radium treatment exerts an immediate very powerful action on myelogenous leukemia when applied over the enlarged spleen for twenty-four hours in relatively large amounts. After three or four applications of from 30 to 33 cg. of radium sulphate, the spleen was found to return to its normal size and the total and differential leucocytic counts to their physiological level, while all the general symptoms disappeared. These effects were noted in 5 cases, all of which had previously been subjected to the Röntgen rays. In 2 patients recurrence took place two and sixteen months, respectively, after cessation of the treatment, and its resumption failed to yield the results previously obtained, possibly owing to insufficient dosage.

This treatment may prove useful in dealing with patients that cannot be removed to the office of the röntgenologist, and is capable of arresting for a considerable time the progress of the disease. In view of the possibility of a difference between the physiological effects of radium and those of the X-ray, the authors suggest that these two agents be tried in alternation or in association. Rénon, Degrais, and Dreyfus (Presse méd., June 18, 1913).

In the first stages of X-ray treatment the leukemic tissues show great degeneration and destruction of the white-cell-forming tissue. This may completely disappear from the spleen, and the process of white-cell formation may be so inhibited that an aleukemic condition of the blood may result. After some months there arises a more undifferentiated leucoblastic tissue, particularly in the retroperitoneal hemolymph-nodes and in the bone-marrow; the leukemic condition of the blood may or may

not return. With an increasing cachexia the process may be terminated by symptoms of intoxication or by some secondary event, as hemorrhage from the necrotic spleen. A. S. Warthin (Am. Jour. Med. Sci., Jan., 1914).

Where neither X-rays nor benzol alone is sufficient to control the disease, the two may be effective when given simultaneously. Edmund Myers (N. W. Medicine, Sept., 1916).

X-ray treatment is the most successful and safest agent. The rays should be directed mainly against the bone-marrow. Treatment of the spleen consists in dividing it into zones of 8 to 10 cm. in diameter; crossfiring is then practised from the front, side, and back. Only 1 area is treated at a time. Arsenic in small doses is advocated where improvement ceases; also in cases with a low red count or the reds and hemoglobin diminishing. H. K. Pancoast (Amer. Jour. of Röntgenology, Jan., 1917).

Radium treatment by surface application is advocated by the writer in cases of leukemia resistant to the X-ray and benzol. The resulting remission may last months or years. Ordway (Boston Med. and Surg. Jour., Apr. 5, 1917).

During treatment of a case of myeloid leukemia with radium and X-rays skin manifestations developed (lymphomas), consisting of numerous slightly nodular lesions, varying in size, slightly raised, soft to the touch, and with a brownish to reddish color, distributed over the chest, back, face, legs and arms. A diagnosis of leukemia cutis was made and the treatment of the underlying condition continued, with resulting recovery from both the cutaneous and general symptoms. I. L. McGlasson (Tex. State Jour. of Med., July, 1922).

Sometimes the general condition improves, but the blood remains definitely abnormal. A few cases are apparently refractory to X-ray treatment.

Thorium X has been administered intramuscularly and subcutaneously

in salt solution. Its action is very similar to that of the Röntgen rays except that it is a little more rapid.

Case of chronic myeloid leukemia treated with thorium X. There was a rapid decrease in the number of leucocytes from 109,000 to 8800 five days after administration of the compound. On the fifty-third day following the injection the white cells numbered 4180. More remarkable than this was the disappearance from the blood of myelocytes, which originally constituted 30 per cent. of the leucocytes. J. Plesch (Berl. klin. Woch., Bd. xlix, S. 930, 1912).

In July, 1912, A. von Koranyi (Berl. klin. Woch., 1912, No. 29) published a case of myeloid leukemia in which very marked improvement occurred following the use of benzol (C_6H_6). There were also reported several cases of benzol poisoning, a striking feature of which was a marked leucopenia. Since Koranyi's paper many other contributions have been added, all showing that benzol causes a preliminary rise in the number of leucocytes, followed by a marked diminution during the second or third week of treatment. The erythrocytes at first decrease, but later they increase, as does also the hemoglobin. The spleen decreases in size, in some cases returns to normal, and the general condition of the patient improves. The lymph-glands are less readily affected. When benzol is used in conjunction with the X-rays the improvement is more rapid than when either is used alone.

From 2 to 5 Gm. (36 to 90 minims) of chemically pure benzol can be given in twenty-four hours, and may be given by mouth or may be injected into the muscles or under the skin. It is best administered in capsules containing 0.5 Gm. (9 minims) each

of benzol and olive oil. In the beginning of treatment a capsule should be given four times a day; later 2 capsules three times a day; then 2 capsules four times a day; and finally 2 capsules five times daily. The rate of increase depends upon the tolerance of the patient and the effect upon the blood-picture. It should not be given when the stomach is empty. Sometimes a burning sensation in the stomach, eructation, vertigo, and a transient tracheobronchitis are observed after its administration. When the leucocytes are diminished to 20,000 per c.mm. the use of the drug should be discontinued, as leucocytic reduction continues for some time afterward. Death may result from the too long continued use of benzol.

Toxic effects observed by Selling as a result of excessive use of benzol were purpura, bleeding from the gums and mucous membranes of nose and pharynx, hemorrhage into the viscera and retina, vertigo, weakness, vomiting, and syncope. The blood-platelets were much diminished, leucocytes almost disappeared from the blood, and the erythrocytes degenerated.

Benzol is a dangerous agent; therefore, its use must be controlled by frequent examination of the blood. In several cases reported the treatment had to be stopped because of the appearance of a red, slightly papular rash, later changing to a reddish-brown color and followed by desquamation. Edema of the eyelids occurred. The urine remained free of albumin.

Case in which X-ray treatment had been without effect, but benzol in doses of 60 drops a day caused a slow but continued betterment in the general condition, splenic enlargement, leucocytosis, myelemla, and anemia.

In the second patient, previously untreated, benzol in the same dose brought about in two weeks a considerable improvement in the general state, with suppression of fever, diminished volume of the spleen, and fall in the leukemia from 300,000 to 80,000 cells. Aubertin (Bull. et Mém. de la Soc. méd. des Hôp. de Paris, May 23, 1913).

The writer gave benzol in doses of 7 minims (0.5 c.c.), increased to 15 minims (1 c.c.), in capsules, after meals and at bedtime, in 5 cases—4 being myelogenous and 1 lymphoid. The results were a rapid fall in leukocytes, resulting in leucopenia in 3 cases; diminution in size of spleen; improved red-cell count and hemoglobin; disappearance of lymphnodes in lymphoid case; improved general condition. The use of drug should be controlled by frequent blood examinations. Billings (Jour. Amer. Med. Assoc., Feb. 15, 1913).

In using benzol in leukemia the writers warn not to carry its effects too far, destroying the function of the bone marrow. The patient ought to be in a hospital, in bed; the alimentary tract, kidneys, and liver, watched carefully; blood-counts made every few days; the dosage not increased without definite warrant, and the benzol stopped considerably before the white count has returned to normal. Barry and Ketchum (Ind. State Med. Assoc. Jour., Aug., 1916).

Report of a striking case in which benzol treatment 7 years before was followed by recurrence 1½ years after cessation of treatment; this recurrence was overcome by further benzol treatment for 4 months, and the patient had been well ever since (nearly 5 years), with normal blood picture. The dose used was 40 drops the first 2 days and 60 to 90 drops daily thereafter for 2 weeks in each month. Vaquez and Yacoel (Bull. Soc. méd. des hôp. de Paris, Aug. 3, 1922).

In the cases in which benzol is not tolerated by the stomach it may be administered subcutaneously or intra-

muscularly in 1.5-Gm. (27-minim) doses with an equal part of olive oil twice daily. Severe burning at the site of injection and in some cases gangrene may occur.

The writers used **benzyl benzoate** in a case of 2 or 3 years' standing. The initial dose was 10 drops of the 20 per cent. alcoholic solution, in water, 3 times a day, after meals, reduced later to 5 drops. When former symptoms recurred the original dose of 10 drops was resumed. Improvement in all the symptoms followed. Haughwout and Asuzano (N. Y. Med. Jour., Aug. 2, 1919).

Acute leukemia sometimes follows septic infections. In a case recorded by Petré-Odin, a prolonged remission was secured by means of injections of **arsphenamin**, 0.6 Gm. doses to a total of 7.2 Gm. being given within a month. Decastello (Wien. Arch. f. inn. Med., Sept. 25, 1925).

Successful results in a case of subacute myeloid leukemia in a boy of 14 years with malaria inoculation. The patient had extreme anemia and fever, with very large and hard spleen and liver. An injection of 3 c.c. of blood infected with *Plasmodium vivax* was given subcutaneously. After 12 malarial attacks the malaria was arrested with 1.5 Gm. (23 grains) of quinine daily. One month later the leukocytes had dropped from 250,000 to 5800, and the red cells had risen from 1,500,000 to 3,880,000, and the hemoglobin from 24 to 52 per cent. The spleen and lymph-glands were markedly reduced and the general condition was progressively improving. T. Lucherini (Policlin., Dec. 14, 1925).

Accidental malaria infection has in 2 reported cases exerted a favorable influence in leukemia. Biñi (Policlin., Jan. 18, 1926).

PSEUDOLEUKEMIA, OR HODGKIN'S DISEASE.

SYNONYMS.—Pseudoleukemia is the term most commonly employed. The terms lymphogranuloma and

lymphogranulomatosis perniciosa have also come into common use.

In the literature of the disease the following are also encountered: Lymphosarcoma (Virchow); malignant lymphosarcoma (Langhans); malignant lymphoma (Billroth); splenic anemia (Strümpell); anemia pseudo-leukemica infantum (v. Jaksch); chronic relapsing fever (Epstein); multiple myelomata (Rusticky); lymphadenoma (Wunderlich); anemia lymphatica (Wilks); adénie (Trousseau).

DEFINITION.—Hodgkin's disease is characterized by enlargement of the lymph-glands and sometimes of the spleen, a progressive secondary anemia, fever, and weakness.

[Hodgkin (Medico-Chirurgical Trans., vol. xvii, p. 69), in 1832, was the first to describe the salient features of the disease in reporting a series of cases, but 2 of which can now be considered as examples of the disease which bears his name. Markham (Path. Trans., vol. iv, p. 177), in 1853, reported a case before the London Pathological Society. The disease seemed to attract little attention until 1856, when Wilks (Guy's Hosp. Rep., Third Series, vol. ii, p. 114) reported a series of cases, after which reports were published by German and French observers. In 1865 Wilks (Guy's Hosp. Reports, xi, p. 56) again wrote upon the subject and named the disease in honor of Dr. Hodgkin. The disease was described under many names by various authors, due to the fact that its nature was unknown. Even today its etiology and pathology are still under discussion. DALAND AND DEVER.]

SYMPTOMS.—In the great majority of cases, and sometimes long before symptoms are recognized, the lymphatic glands begin to enlarge. Usually the first evidence appears in the submaxillary glands or those in the posterior cervical triangle. In a series of cases

reported by Gowers the order of frequency of affection of the other glands was as follows: (a) Axillary; (b) inguinal; (c) bronchial; (d) mediastinal; (e) retroperitoneal. If the glands in the thorax or abdomen are the first to enlarge, the primary evidence of the disease may be pallor and symptoms due to pressure. These cases present great difficulty in diagnosis.

Case in a woman of 62 years, with enlarged lymph-nodes on both sides of the neck, in the axillary, epitrochlear, inguinal, right popliteal and right preauricular regions. The blood showed erythrocytes, 3,400,000; leucocytes, 8000; hemoglobin, 65 per cent. Metastasis in this disease is regarded only as a proliferation of preëxisting lymphoid tissue. J. Loudon (Canad. Jour. of Med. and Surg., Aug., 1922).

Paraplegia and cauda equina symptoms observed in Hodgkin's disease in a boy of 19 years. The author refers to 4 other similar cases in literature. F. P. Weber (Quart. Jour. of Med., Oct., 1923).

Four cases of herpes zoster occurring in Hodgkin's disease. One patient died, the zoster occurring rather late in the affection. In 4 cases still under observation, the zoster occurred rather early in the disease in 3 and late in the other. Seemingly, the severity of the disease had nothing to do with the eruption, but the herpes was probably due to irritation caused by the mass of glandular enlargement in close proximity to the ganglion. Pancoast and Pendergrass (Amer. Jour. Med. Sci., Sept., 1924).

The glands are usually discrete, firm, smooth, and freely movable. Aggregations of nodes may be bound together by loose connective tissue to form huge masses. The glands on one side of the neck may be enlarged for some time before those on the opposite side show involvement. Not uncommonly the disease is seen to advance from the cervical to the su-

praclavicular and axillary nodes on the same side before those on the opposite side are involved. When the submaxillary glands are the first to show disease, extension to the opposite side is more rapid. The enlarged glands may encircle the neck and interfere very materially with the movements of the head. The swellings often invade the mastoid and occipital regions. Sometimes after a group has enlarged, diminution in size occurs and the disease apparently becomes quiescent. It then may burst forth suddenly and terminate rapidly in death. Pain does not accompany the enlargement of the glands and when present is due to secondary inflammatory changes or to pressure upon nerves. Secondary pressure effects are very common. Mastication may be interfered with by the huge mass of cervical glands. Pressure upon the esophagus may cause dysphagia, and in rare instances complete occlusion may occur.

Anemia of the brain may be caused by pressure upon the carotid arteries, in which event tinnitus aurium, dimness of vision, and vertigo upon slight exertion may be observed. If the growth exerts sufficient pressure to further diminish the amount of blood distributed to the brain, irregular breathing occurs, and convulsions, coma, and even death follow. Deafness is a common symptom due to pressure upon the Eustachian tube. Very pronounced cardiac irregularity may be the result of pressure upon the vagus.

A laryngoscopic examination may reveal paralysis of a vocal cord as a result of interference by the enlarged glands with the recurrent laryngeal nerve. In some cases it may be im-

possible to make a satisfactory laryngeal examination because of the displacement of the larynx by the masses. Pressure upon the trachea or bronchi causes cough and dyspnea. Some cases show edema and cyanosis of the head, face, and arms due to compression of the superior vena cava. A unilateral or bilateral pleural effusion may be present, due to direct irritation of the pleura from enlarged glands or from compression of the azygos or bronchial veins.

Severe pain with edema and cyanosis of the arms may result from pressure exerted by greatly enlarged axillary nodes. A similar disturbance may result in the legs as a result of pressure exerted by the inguinal, pelvic, or retroperitoneal glands. Sciatica is sometimes thus produced. If the common bile-duct is obstructed, jaundice will be noted. Secondary growths may occur in the lungs, causing cough and expectoration. Nausea, vomiting, and diarrhea may be caused by involvement of the lymphoid tissue of the gastrointestinal tract. Ulceration in the stomach or intestines may cause hematemesis or melena. Constipation may be due to pressure upon the sigmoid or rectum; complete obstruction anywhere along the intestinal tract is very rare.

Secondary growths of lymphatic tissue may occur in the liver and kidneys, but rarely cause symptoms. The spleen, though it never reaches the enormous size found in leukemia, is enlarged in many cases. The enlargement is not associated with pain. Pruritus may be a very annoying symptom. Bronzing of the skin, suggesting Addison's disease, occurs in some cases and is ascribed to pressure of enlarged glands upon the

celiac plexus. This discoloration of the skin occurs even without involvement of the adrenals. It is sometimes observed after the prolonged administration of arsenic. Masses of lymphoid tissue may enlarge in unusual places in the skin.

The writer agrees with Ziegler and Westphal that from 15 to 25 per cent. of cases show skin lesions. Pruritus is commonest, and next, an exanthem of pruriginous type, most often present on the extensor surfaces. Urticaria is also fairly common and edematous swellings are seen. Pigmentations are frequent.

Alopecia, dryness of the skin, atrophy, and hyperkeratosis are not uncommon.

Icterus and purpuric lesions are less frequent. Reddish or bluish tumors in the skin constitute the condition called "lympho-granulomatosis cutis." H. N. Cole (Jour. Amer. Med. Assoc., Aug., 1917).

Fever is present in the majority of cases. It may be irregular in type and is sometimes absent for considerable periods. On the other hand, there may be a continuous mild fever (100° to 102° F.—37.8° to 38.9° C.) throughout the course of the disease. The morning temperature may be normal or subnormal and the evening temperature 102° to 103° F. (38.9° to 39.4° C.). Pel and Ebstein have described cases in which relapsing fever occurred, the febrile period lasting about a week, followed by a period of apyrexia of ten days to two weeks' duration.

Blood examinations reveal a progressively increasing secondary anemia. The erythrocytes are reduced to 2,000,000 or less per c.mm. and the hemoglobin below 40 per cent. in late cases. The anemia may become extreme. Often there is no increase in the number of leucocytes, though they

may number 25,000. The polymorphonuclear leucocytes usually number 70 per cent., and a higher percentage is found in cases in which secondary infection has taken place in the glands. Sometimes an increase in the lymphocytes is found. In a few cases the eosinophiles are increased.

The urine is usually negative. When fever is present, especially when above 103° F. (39.4° C.), albuminuria is common.

DIAGNOSIS.—This is often difficult to establish without a histological study of an excised gland. Hodgkin's disease may resemble glandular tuberculosis so closely that a differential diagnosis cannot be made clinically. A tuberculin test often assists very much in making the diagnosis; but it is to be remembered that the reaction may not appear in the cachexia of advanced tuberculosis. It must also be remembered that Hodgkin's disease and tuberculosis are very frequently associated.

Lymphoid leukemia may be confounded with Hodgkin's disease. A careful blood examination, including a differential leucocyte count, will make the diagnosis clear.

It is impossible, occasionally, to differentiate clinically Hodgkin's disease from lymphosarcoma. The histological pictures of the glands are distinctly different in the two conditions. In Hodgkin's disease the gland contains an increased amount of connective tissue, and three types of cells, viz: lymphoid cells, giant cells with one or more nucleolated nuclei, and in most cases eosinophile cells. In lymphosarcoma the mass is composed of a delicate reticulum in the meshes of which lie cells rather larger than lymphoid cells. It penetrates the cap-

sule and invades the adjacent tissues. When the diagnosis is not clear, a superficial lymph-gland should always be removed for histological study. This can be done readily under local anesthesia, without detriment to the patient.

ETIOLOGY.—The cause of Hodgkin's disease is still in doubt. Formerly the disease was thought to be a malignant growth by some observers including Coley.

Hodgkin's disease must be classed with the lymphosarcomas and endotheliomas of the lymph-nodes as a neoplastic process. The following facts compel this conclusion: (a) The similarity, and in cases identity, of the histological process; (b) the early and constant development of malignancy (invasion of capsule and veins); (c) the ultimate formation of true metastases, partly at least by the blood-stream. Oliver (Jour. of Med. Research, Dec., 1913).

Research suggesting that the causal agent is probably a polymorphous fungus which locates in the lymph glands. It can be cultivated from them and is pathogenic for animals. Cultivation on Sabouraud's saccharosed gelose succeeded in about 50 per cent. of the inoculations, the growth with one type of the germ resembling that of cultures from actinomycosis. The other principal type is more bacilliform in aspect and cultures. These differences are more marked at first than later, in time all the cultures resembling each other. The rat, guinea-pig, rabbit and monkeys are susceptible to the germ, and all die sooner or later when inoculated in the peritoneum, although the experimental disease may last for a month or more. The provisional name of the germ is *Adenomyces crusi*. Dias (Brazil Medico, Sept. 1, 1917).

It is generally believed now that it is an infection, and this belief is supported clinically and histologically.

Sternberg (Zeit. f. Heil., xix, 21, 1898) stated that the disease was a special form of glandular tuberculosis. Since then investigators have brought forth evidence that disputes his view.

[Dorothy Reed (Johns Hopkins Hosp. Reports, x, 133, 1902) and Longcope (Bull. Ayer Clin. Lab. of Penna. Hosp., No. 1, 1903) have shown definitely that Hodgkin's disease and tuberculosis are separate affections. Both processes may, however, occur simultaneously.]

Fraenkel and Much (Zeit. f. Hyg. u. infect. Krankheit., lxvii, 159, 1910) found an organism greatly resembling the tubercle bacillus in 12 out of 13 cases of Hodgkin's disease which were clinically and anatomically free from tuberculosis. The organisms appeared as granular rods, which resisted antiformin, stained by Gram's method, but were not acid-fast. Notwithstanding the absence of clinical and pathological evidence of tuberculosis in the cases, they concluded that, if the organisms found were not actually tubercle bacilli, they were at least closely related to them.

Negri and Miermet (Centralbl. f. Bakt., etc., lxviii, 292, 1913) confirmed the findings of Fraenkel and Much, but stated that the organism was not related to the tubercle bacillus, but was a diphtheroid organism which belonged to the species *Corynebacterium* and suggested the name *Corynebacterium granulomatis maligni*.

In August, 1913, Bunting and Yates (Arch. Int. Med., vol. xii, 236, 1913) confirmed the findings of Negri and Miermet and agreed with them in the classification of the organism. They suggested the name *Corynebacterium Hodgkini*. The organism is described by them as a non-acid-fast, Gram-staining bacillus, which grows luxuriantly at body temperature and which is a facultative anaërobe. It may occur as plump, short rods, which may closely resemble cocci-bacilli; small, thin bacilli with polar-staining, comma-shaped bacilli; granular rods of variable size; branching forms; club-shaped involution forms, and large, spherical forms. The same investigators (Jour. Amer. Med. Assoc., lxi, 1803, 1913, and Jour. Amer. Med. Assoc., lvii, 516, 1914), by inoculating

monkeys with the organisms, were able to produce in the lymph-nodes a chronic lymphadenitis with a typical proliferation of the endothelial cells and stroma, and a well-marked eosinophilic infiltration. The corynebacterium was also isolated from the lymph-nodes in 12 cases of Hodgkin's disease by Billings and Rosenau (Jour. Amer. Med. Assoc., lxi, 2122, 1913), and Kusunoki (Virchow's Archiv, ccxv, 184, 1914) found them in 16 cases. DALAND AND DEVER.]

The writers were led to conclude from the finding of ameboid cells closely resembling *Endamaba dysenteriae* in the bowel as well as in the lymphatic glands that Hodgkin's disease is an amebiasis of the lymphatic system. The types of mitosis in the observed cells are held to have particular differential value. Kofoid, Boyers and Swezy (Jour. Amer. Med. Assoc., May 27, 1922).

There is a dysenteric prelude in a large number of Hodgkin cases. Intestinal symptoms should be given more attention, and the stools examined. The author reports a case of malignant lymphogranuloma beginning 4 months after amebic intestinal infection, with involvement of the glands of the right side of the neck and later typical course of Hodgkin's disease. In the stools Kofoid later found *E. dysenteriae*. **Neoarsphenamin** in 0.9 Gm. doses was given intravenously, **emetine hydrochloride**, $\frac{1}{2}$ grain (0.03 Gm.) hypodermically twice daily, with daily cleansing **enemas** and **ipecac** by mouth. A significant prompt improvement followed. Lambright (Jour. Amer. Med. Assoc., Sept. 2, 1922).

Out of 191 cases, only 8 showed evidences of tuberculosis in Roentgenograms of the chest. A like number of unselected cases revealed evidence of tuberculosis in 17 instances, tending to show that tuberculous mediastinal glands are relatively uncommon in Hodgkin's disease. W. S. Lenion (Amer. Jour. Med. Sci., Feb., 1924).

The disease occurs most commonly in males and usually before the fortieth year. In W. T. Longcope's series of cases the youngest patient

was 7 and the oldest 35 years of age. It may be that the disease enters through the tonsils, gums, or mucous membranes of the nose or throat. The disease first shows itself in the majority of cases in the cervical glands. There is no evidence that heredity, bad food, exposure to cold or wet, impure air, etc., play any rôle in the production of the disease.

The duration of Hodgkin's disease varies from a few months to several years. An exact study of the duration is not possible because of the difficulty of determining the exact time of onset. The disease may exist for many years without more than slight enlargement of a single group of glands. Then, suddenly, general glandular enlargement, with pronounced constitutional symptoms, may occur, followed by death in a few months. In reckoning the duration of the disease, therefore, it may happen that the acute exacerbation only is considered.

Generally the disease is chronic, though acute cases causing death in a few months do occur.

[Gowers (Reynolds's "System of Medicine," Phila., 1879) in a study of 50 cases found that in 18 cases the duration was less than one year; in 15 cases between one and two years; in 6 cases between two and three years; in 6 cases between three and four years; in 3 cases between four and five, and over five years in but 1 case. It seems from this study that most cases die before the third year. The average duration of the whole 50 cases was nineteen months. DALAND AND DEVER.]

The most common cause of death is asthenia. The patient becomes more and more anemic, edema and finally anasarca occur, dyspnea increases, weakness becomes more pronounced, and finally death ends the scene.

Sometimes death occurs suddenly. In some cases starvation due to compression of the esophagus hastens the fatal termination. Death may occur from suffocation due to compression of the trachea.

Intercurrent infections commonly occur and shorten the life of the patient. Pneumonia is common; infection with the tubercle bacillus is very common. Often a group of enlarged glands may be thus infected and, caseating, may discharge pus. Miliary tuberculosis may occur.

PATHOLOGY.—*Lymph-glands.*—Enlargement of one or more groups always occurs, forming lobulated masses composed of discrete nodes bound together by connective tissue. They almost never fuse. The nodes may be soft or very firm, and glands of different consistency may be present in the same group. Sometimes they give a sense of fluctuation, but on incision no fluid is found. The masses are not bound to the skin or adjacent structures and are movable under the skin, unless by their size they have stretched the skin too tightly over them to permit of motion. Necrosis occurs only when secondary infection occurs. On section the appearance varies with the age of the growth. The older growths present a semi-translucent, grayish surface, divided by intersecting lines of yellowish fibrous tissue. The younger growths present a uniform, grayish, bulging surface, somewhat more opaque than normal.

Microscopically, the appearance varies with the age of the growth. In the youngest glands dilatation of the blood-vessels and lymph sinuses is well marked, with proliferation of the flat endothelial cells of the reticulum

of the latter. Later, the lymph sinuses become filled with lymphocytes, usually of the small type, and proliferating endothelial cells, destroying the normal appearance of the gland.

Large epithelioid cells with vesicular nuclei are formed from the proliferating endothelial cells. Many giant cells with one or more nuclei are found. Eosinophiles are usually present in large numbers. As the masses become older the fibrous tissue proliferates, dividing the gland into sections and destroying many of the pre-existing cells. In old masses the connective tissue may be observed in greater amount than the cellular tissue. Rarely the cells of the gland penetrate the capsule. When they do so, they do not invade the surrounding tissue in all directions, but push the tissue cells in front of them, forming a dense border simulating a capsule.

The connective tissue which is so characteristic of the older growths is the result of proliferation of the connective tissue about the blood-vessels. It also develops from the endothelial cells which line the tissue spaces. These cells, in proliferating, form giant cells with one or more nuclei. There may be as many as 10 nuclei in a single cell. Some of the nuclei contain nucleoli. These giant cells are peculiar to Hodgkin's disease.

Metastatic nodules may occur anywhere in the body. They have the same appearance as the tissue of the enlarged glands. As they enlarge, the cells of the organ or tissue in which they grow are pushed aside and flattened out, forming an apparent capsule.

Spleen.—Slight enlargement is often found. Rarely does the organ attain great size. It is firm, preserves the normal contour, and is smooth except

when protrusion of metastatic growths causes the surface to be nodular. On section it is red, purple, and grayish white.

The *liver* may be slightly enlarged, though very frequently no abnormality may be detected. Secondary growths may be present.

The other organs of the body, as a rule, present no changes, except that they may be the seat of metastatic growths.

PROGNOSIS.—As far as known, Hodgkin's disease is always fatal. Patients rarely live more than three years after symptoms become pronounced. As stated, the glands may enlarge and remain so for several years before the patient is conscious of abnormal subjective sensations. Sometimes after a group of glands have been enlarged, diminution in their size may occur, followed by a longer or shorter period of latency.

Death occurs usually from cachexia or is the result of secondary infection. Lobar and lobular pneumonia are frequent complications that hasten death. Tuberculosis is a very common complication. It may occur in a group of affected glands and later become disseminated throughout the entire body. Anemia rarely causes death. Suffocation from pressure on the trachea may be the cause of death. Death from inanition is apt to occur in those cases in which the glands in the neck interfere very materially with mastication, and in those cases in which the ability to swallow food is greatly diminished.

TREATMENT.—Up to the present time no treatment has been effective in saving the life of the patient. Surgical treatment should not be considered except when it is neces-

sary to relieve pressure symptoms that threaten life.

Early diagnosis of Hodgkin's disease is urged. Portals of entry of infection should be sought and eliminated, as by tonsillectomy, healing of chronic cutaneous or mucous membrane lesions, care of the teeth and accessory sinuses, and cure of enterocolitis or constipation. **Early extirpation** of all accessible **enlarged glands** should also be practised, followed at once by prolonged **Röntgen-ray treatment** of the operative field and of all glands not removed. All efforts should be made to improve general health. **Immune serum** should be given for its general and specific effects. Medication may be helpful as a general measure. Excision for diagnosis should never be tried unless one is prepared to make it complete if a frozen section proves positive, as this procedure accelerates the disease. Upon the treatment mentioned, recovery for over 5 years is estimated to occur in less than 5 per cent. of acute cases; 80 to 90 per cent. of incipient chronic cases; 60 to 70 per cent. of early chronic, and 5 to 10 per cent. of advanced and rebellious chronic cases. Yates and Bunting (Jour. Amer. Med. Assoc., Mar. 10, 1917).

Arsenic has been the favored drug, Fowler's solution being given in ascending doses. It is of little service and may be harmful in those cases in which gastrointestinal disturbances follow its use. **Sodium cacodylate** may be used in 1- to 5-grain (0.06 to 0.3 Gm.) doses, hypodermically, on alternate days.

Since 1902 the **Röntgen rays** have been employed, without, however, effecting a cure. Life has been prolonged four or five years from the onset of treatment. Under this treatment the enlarged glands gradually diminish in size and the general state of health improves. If the spleen is

enlarged, it likewise decreases in size. The lymph-glands rarely, if ever, entirely disappear; usually they are felt as masses about the size of a pea.

The life expectancy should be greatly increased by intensive **radium** treatment of the superficial glandular enlargements and **deep X-ray** therapy of the thoracic and abdominal cavities, whether the roentgenograms are positive or not. Huge glandular enlargements and mediastinal involvements are markedly diminished. For radium treatment the writer uses 50 or 100 mgm. of the salt or emanation, contained in brass or silver capsules and also filtered through lead, held 2.5 cm. from the skin for 10 or 20 hours. Two to 4 areas are usually radiated at one time, at intervals of 2 or 3 days. For X-ray treatment the chest is divided into 4 areas and the back into 8, and exposures repeated every 3 weeks until 6 or 8 treatments have been given, followed by a 3-month interval. The X-ray treatments are usually given at the beginning or at the end of the radium exposures. Bowing (*Jour. of Radiol.*, Dec., 1921).

Study of the histories of all patients entering the Mayo Clinic between 1915 and 1920 in whom a definite diagnosis of Hodgkin's disease or lymphosarcoma had been made by microscopic examination of excised glands. There were 135 cases of Hodgkin's disease, of which 92 could be traced; of these, 10 were living and 82, dead. There were 102 with lymphosarcoma; of these 76 could be traced; 9 were living and 67, dead. The data indicate that men are 2.3 times more susceptible to Hodgkin's disease than women, while lymphosarcoma attacks men 4.4 times more often than it does women. The period of greatest susceptibility to Hodgkin's disease is from the 2d to the 5th decades, with emphasis on the 3d and 4th. Lymphosarcoma is most prevalent during the 3d to the 7th decades, particularly the 5th and 6th. There is a close similarity in the symptoms. The average duration of Hodgkin's disease in 73 cases was 2 years

and 7 months; in 55 cases of lymphosarcoma, 2 years and 5½ months. While it was not possible to show that systematic treatment by **X-rays** definitely prolonged life, such treatment kept the disease under complete or partial control for varying periods. Desjardins and F. A. Ford (*Jour. Amer. Med. Assoc.*, Sept. 15, 1923).

The glands often enlarge rapidly when treatment is suspended.

In some instances after treatment is discontinued, the glands continue to decrease for a short time. A recurrence is sure to take place and finally the disease causes the death of the patient.

Apart from the usual manifestations in connection with the lymphopoietic organs and even after their entire disappearance following X-ray therapy, other visceral or bony localizations may supervene which form an integral part of the disease. The bony lesions are sometimes latent and must be sought by careful X-ray examination. They must not be confused with bone tuberculosis or with true bone neoplasms, which they resemble. They are amenable to **X-ray therapy**, methodically applied. Bécélère (*Bull. Soc. de radiol. méd. de France*, July, 1924).

Benzol has been tried with apparent benefit in a few cases.

Benzol, 5 minims (0.3 c.c.), three times daily at first, then increased to 10 minims (0.6 c.c.), caused marked regression of enlarged nodes, beginning two weeks after treatment was begun, in a case previously treated unsuccessfully with X-rays. The 10-minim (0.6 c.c.) dose was continued 6 weeks. Lawson and Thomas (*Jour. Amer. Med. Assoc.*, Dec, 13, 1913).

JUDSON DALAND

AND

FRANCIS J. DEVER,
Philadelphia.

LEUCOPLAKIA. See TONGUE,
DISEASES OF.

LICHEN PLANUS.—DEFINITION.—Lichen planus is an inflammatory disease of the skin in which small, flat, angular, red or bluish-red, shining papules form. These occasionally coalesce and form patches. A variable amount of itching is present. Lichen acuminatus, though formerly considered a variety of the same disease as lichen planus, is now generally conceded to be identical with the pityriasis rubra pilaris of Devergie.

SYMPTOMS.—This eruption begins as small, reddish papules, which become angular, polygonal, or faceted. These papules are red and shining and sometimes show a depression or umbilication due to a glandular orifice present in the center of the papule. The color of the papules may be pinkish red, violaceous, or purple. On the grayish, translucent surface of the papule one may distinguish grayish striae. Scaling is usually absent. The papules may be discrete, but are more often in patches, sometimes arranging themselves in rings (lichen planus annularis), sometimes in lines, and when a beaded linear formation predominates it is called lichen ruber moniliformis. The favorite sites of the eruption are the flexor surfaces of the wrists and arms, although the abdomen, legs, and the back of the hands may be affected. Large areas of the body may be involved.

The eruption of lichen planus appears gradually. Its duration is variable, and, while relapses occasionally occur, distinct second attacks are not common. A brownish pigmentation, which slowly fades, is left after the eruption disappears.

DIAGNOSIS.—The peculiar features of the eruption, its distribution, and the absence of previous moisture will differentiate this affection from eczema. The purple or lilac tint of infiltrated plaques on the legs and the outlying discrete papules will distinguish this disease from psoriasis or eczema.

ETIOLOGY.—Nervous exhaustion is the most common cause, but digestive disturbances seem causative in some cases. Lichen planus is rare in children; it is pre-eminently a disease of adult life.

PROGNOSIS.—This is favorable, but the course of the disease often extends over months.

TREATMENT.—**Hygiene** and diet are important elements in treatment. **Arsenic** is most useful in the subacute and chronic cases. **Mercury** is frequently a valuable remedy. In **Donovan's solution** (liquor arseni et hydrargyri iodidi) the two are combined. **Salicin** in 15- to 20-grain (1 to 1.3 Gm.) doses was recommended by Crocker in subacute and chronic cases; **potassium chlorate**, **dilute nitric acid**, and **quinine** have also been advised in these same cases. **Change of climate** is often curative. Among the local remedies may be mentioned **tar**, **phenol**, **menthol**, **chrysarobin**, **salicylic acid**, and the **mercurials**. Some cases yield best to the **X-rays**.

LICHEN RUBER ACUMINATUS (PITYRIASIS RUBRA PILARIS).

SYMPTOMS.—This is a cutaneous inflammation marked by small, conical, dry papules with horny centers, occupying the mouths of hair-follicles, running a chronic course, and gradually tending to extend. The three characteristic points of this eruption are horny, follicular papules, pityriasic desquamation, and exaggeration of the natural folds of the skin.

The eruption may first appear on the palms, soles, scalp, or face, giving rise to generalized redness with roughness and scaling. On the scalp it simulates dry seborrhea. On the face fine, adherent scales are found in the frontal, orbicular, and nasolabial regions. The papules are pale yellow, pale red, or of duller hue, and are generally pierced by hairs. Surrounding the hair and penetrating the follicular opening is a horny sheath. A horny plug may occupy the center of the papule. Large areas may be involved. The papules may coalesce and form patches. Horny, black plugs are generally present upon the backs of the first digital phalanges and at the nape of the neck. Itching may be present. The course is chronic, subject to exacerbations, and may terminate in pityriasis rubra. Death from the disease sometimes occurs.

ETIOLOGY AND PATHOLOGY.—The cause of the disease is obscure. It is a disease of childhood and early adult life.

Cornification of the epithelial layers around the mouths of the hair-follicles

produces the horny papule. Follicular hyperkeratosis is the essential lesion. Chronic inflammatory changes in the corium are found in prolonged cases.

PROGNOSIS.—A fatal issue is rare. Recurrence may follow apparent cure. The course of the disease is a very slow one, sometimes ending in recovery, but usually persisting for an indefinite time.

TREATMENT.—The treatment of this affection is that used in psoriasis. The remedies advised are **arsenic, mercury, pilocarpine, thyroid extract, and tonics. Alkaline baths, salicylic acid, tar, pyrogallol, chrysarobin,** depending upon the stage of the disease, are used locally. The general health should not be neglected.

LICHEN SCROFULOSUS.

SYMPTOMS.—This is a chronic inflammation of the skin in which occur flat, reddish or yellowish, more or less grouped, scaly papules, about the size of a millet seed. It affects scrofulous persons, especially the young. The papules originate about the hair-follicles, and are scattered over the chest and abdomen. The course is chronic. The affection is rare.

TREATMENT.—The indications are for **good food and personal hygiene. Cod-liver oil,** internally and externally, will generally cure the disease.

LICHEN TROPICUS. (See **MILIARIA**, this volume.) W.

LIGHT THERAPY, OR HELIOTHERAPY.

Light therapy properly employs all of the effects of radiant energy except the higher frequencies of the Röntgen ray as affecting the tissues of the organism. *Heliotherapy*—radiant energy from the sun—would, under the present understanding of this department of therapeutics, comprise but a relatively small part of the subject, since the employment of high-candlepower lamps provided with reflectors and lamps of lower capacity, both arc and incandescent, is quite as effective in therapeutics as the sunlight, and more

convenient and not so capricious as the emanations from the sun in most climates.

Radiant energy emanating from any luminous source comprises, besides the visible rays, the radiations of higher and lower frequencies—*ultra-violet* and *infra-red*. From the various sources, natural and artificial, the proportions of different frequencies will vary. The emanations from the sun are rich in all the frequencies, as are also the emanations from the arc light. The radiations from carbon-filament incandescent lamps are rich in all of the frequencies except the ultraviolet. The tungsten-filament incandescent lamps are less rich in the lower frequencies and void of the ultraviolet, but decidedly rich in the luminous rays.

Light in transmission from incandescent bulbs, which is of necessity produced within the glass container, loses the higher frequencies, by being filtered out in their passage through the glass wall of the lamp.

Arc lamps are manufactured with rock-crystal lenses or windows, as were the lamps of Niels Finsen, because they permit the passage of the ultraviolet rays. These lamps are employed particularly for administration of the ultraviolet radiations. The effects of these rays are superficial, producing intense hyperemia and tanning of the outer layers of the skin, and do not penetrate the vascular layers unless they are rendered anemic, as first demonstrated by Finsen.

It must be understood that the effects of radiant energy as affecting the tissues of the body are derived from the transformation of this energy or its conversion into heat or other

forms of energy in the tissues. Again, the physiological effects of the forms of radiant energy must be considered complexly as to the effects of the different frequencies upon the tissues or upon germs or other organisms resident in the tissues. From this point of view the therapeutics of radiant energy has developed an exceedingly important field.

PHYSIOLOGICAL ACTION.—

The physiological effects of radiant energy vary with the intensity and volume of the radiations which penetrate the tissues to a considerable depth. Kellogg has stated that radiant light penetrates fully 6 inches within the tissues. The penetrations of the various wave lengths are unequal. The red and infra-red radiations penetrate deeper into the tissues than the luminous rays and higher frequencies, the radiations of longer wave length and lower frequency having the greater power of penetration. It will be understood, therefore, that the deeper effects of radiant energy are derived from the infra-red radiations producing heat in the tissues relative to the volume of the radiations.

The degree of penetration varies considerably, however, with the color of the skin of the individual. In brunettes, and to a greater degree the negro, the radiations are absorbed in the pigmented layers of the skin and the penetration to the deeper tissues is relatively less. For this reason the intense effects due to absorption of the radiations in the skin cause the sweat-glands to become more active and the perspiration more profuse. This remarkable provision of Nature protects the dark-skinned inhabitants of the tropics from the overstimulating

effects of radiant light in the deeper tissues, and coincidentally the evaporation of the increased perspiration by the latent heat of evaporation produces a marked lowering of the peripheral temperature, especially so when in a dry atmosphere the evaporation takes place promptly. This affords great relief from the thermic effects of the sun's rays. A person having dark-colored skin for the same reason receives very little benefit from therapeutic administration of radiant light and heat, the penetration being proportionate to the degree of pigment in the coloring matter of the skin. For this reason tanning of the skin by the sun's rays by the radiations of the electric arc prevents the therapeutic effects reaching the deeper tissues when indicated.

The **electric arc** and other sources of radiant light, including the sun, which are rich in ultraviolet radiations, produce tanning and are therefore not so practical for therapeutic applications other than in the most superficial disorders. When the prolonged use of radiant energy is indicated the tanning, after the first applications, prevents the full effect of the other radiations to the deeper tissues. The ultraviolet radiations, however, play a most useful rôle in Nature in that they destroy germ life exposed to them in the atmosphere, in water which they freely penetrate, and on surfaces everywhere. It must be borne in mind, however, that they do not penetrate glass, and, therefore, that they do not sterilize the house air, excepting through the open window. Furthermore, these rays act only on the outer layers of the human skin. In the **incandescent light**, these rays being filtered out by the glass wall of

the bulb, the objectionable feature is removed and the light is rendered practical for its general thermic and other valuable therapeutic effects. This has been demonstrated by numerous observers to their satisfaction in the treatment of various infections and other conditions in which radiant energy is indicated.

The **thermic effects** of radiant energy derived from the various sources arise from its transformation into the lower frequency of heat vibrations in the tissues, and are effective as far as they penetrate for both local and general effects.

The **local effects** are to induce as far as the light penetrates a degree of hyperemia, which will vary with the volume of radiations, the toleration of the patient to whom the radiations are applied, and the length of the application.

General Effects.—Added to the local effect, the blood, warmed as it passes through the heated field exposed to radiant energy, conveys a glow of warmth throughout the whole body, producing general perspiration and otherwise increasing general metabolism. When such applications are made for a considerable time the secretory and excretory functions of the body are accelerated, particularly so throughout the exposed parts of the body to which the application is made. General metabolism is thus quickened and increased activity of the normal processes of the whole organism is thus engendered. In addition to these thermic effects of radiant energy, there are undoubted influences of light tending to a gradual increase in the red cells in anemic patients. As great an increase as 1,000,000 per c.mm. has been noted by

the writer in one month, which could be attributed to no other cause.

The **actinic effects** of the luminous radiations, though to a less degree than of the ultra-violet, have a marked inhibitory action upon most forms of germ life. Particularly susceptible to these are the pyogenic bacteria and other bacteria which are sensitive to light, for which reason radiant light plays an important therapeutic rôle in the treatment of conditions characterized by their presence as an exciting cause of local inflammation.

THERAPEUTICS.—Accordingly, the therapeutic indications for radiant energy include (1) the treatment of defective local and general metabolism; (2) local repair of impaired or injured tissues, and (3) removal from the tissues of some types of infection, particularly the pyogenic bacteria.

While its effects upon **general metabolism** may be derived from the gradual heating of the blood-stream during local application, the liberal administration by light baths or extensively by high-candlepower lamps to the trunk or large portions of the body at each application is remarkably effective. In **anemia** or in those in whom **autointoxication** is manifestly present with **impairment of the excretory and secretory functions** of the body, general applications are invaluable, the effect being to stimulate profuse perspiration and to quicken all of the emunctory functions.

Radiant energy is not effective for the relief of densely congested areas the seat of extreme conditions of local stasis, applications to which afford but temporary relief from pain due to relaxation of local tension or pressure.

In **local infection**, when the presence of germs is the exciting cause of in-

flammation, application of radiant light and heat is especially efficacious. Especially is this the case in that very large number of such conditions wherein the depressing influence of radiant energy upon germ life and the induction of hyperemia in the field of infection, through which a large number of phagocytes attack and destroy the germs present, are brought actively into play. There are few forms of **pyogenic infection** which, before pus appears, cannot be aborted by energetic applications of radiant light and heat.

It is important that the applications should be made near enough to the surface that a degree of heat is projected which cannot be tolerated unless the therapeutic lamp is moved about rapidly over the surface of the infected part. Furthermore, applications should be made for a long time—for one-half to one hour. In acute conditions where infection is severe, applications should be repeated every few hours until there is complete subsidence of the inflammation, indicating a destruction of the germs in the local field. In some cases, as in **acute otitis media**, relief of pain will be a fairly good indication of the cessation of active germ proliferation.

The local infections in which radiant energy is indicated are at present not fully determined. It is safe to say, however, from the point of view of the writer, that it is contraindicated in no condition in which infection is present except when a lesion is under treatment with the X-ray, which produces directly opposite effects. Experience has demonstrated its great value in the treatment of those cases in which streptococci, staphylococci, and the other forms of pyogenic bac-

teria are actively proliferating, when applied before pus forms or after the local evacuation of pus, in which cases it is possible to abort the infection if employed with energy soon after the onset of pain.

In **acute otitis media** the application should be instituted at the outset and made by rapidly moving the light over the ear and surface surrounding it until there is complete cessation of pain, repeating the application if there is a recurrence of pain. By this method the trouble will be promptly arrested and cured if pus had not already formed.

In **chronic otitis media** with a purulent discharge it is possible in all cases except when the ossicles are necrosed to cure the condition within a short time by one or two daily applications. No measure in therapeutics will give greater satisfaction than the use of radiant light and heat in otitis media. It may be applied from a fifty candle-power incandescent therapeutic lamp, the exposure being made for from one-half to one hour once or twice daily.

In **early cases of mastoiditis** it will always be safe to employ radiant light pending an operation, when, if pain is relieved and blood examination shows a lowered phagocytosis, an operation will be unnecessary.

In the treatment of **carbuncles**, **boils**, and **felons** the same principle of application and method as employed in the treatment of otitis media will succeed in nearly every instance before pus has formed. Likewise the **early cases of appendicitis** may often be arrested and aborted by this same measure. The writer has observed temperatures present with acute appendicitis to fall from 1° to $2\frac{1}{2}^{\circ}$ F.

in twelve to twenty-four hours under the application of radiant light and heat with arrest of the active process. In **suppurative tonsillitis** when applied in the same manner as in otitis media it is equally effective.

In **erysipelas**, in which the writer has had an opportunity of employing radiant light and heat, in but 3 cases has it proved satisfactory. These cases were treated at the onset and the applications were made for one to four hours, no administration being made for less than one hour in the manner described. The result in each case was complete arrest of the erysipelatous condition. In one case the edema of the face had closed both eyes. After four hours' exposure to intense radiation—two hours in the morning and two in the afternoon—the edema disappeared. Two additional exposures on the two following days restored the features to normal.

In **acute coryza** during the past winter it has been demonstrated that applications from carbon-filament incandescent therapeutic lamps, as employed in other conditions, for from one to one and one-half hours, of radiant light in the early stage of the condition, have invariably arrested and cured the cases so treated. Likewise in **acute and subacute laryngitis**, when employed preceding the static wave current locally applied, it has been possible to arrest all cases in the early stage and to relieve advanced cases, including cases of **clergymen's and singers' sore throat**. The light in these conditions probably has a two-fold effect, one upon the circulatory condition and the other upon the germs which may be present as the exciting cause.

In **phlebitis and varicose ulcers**

radiant light and heat singly after repeated applications relieves many severe cases. When followed at each séance with a systematic application of the static brush discharge the cure is more promptly effected.

In **mastitis** before pus is formed prolonged applications of radiant light and heat will effectively dissipate the inflammation, and after pus forms, following its evacuation, they will promptly restore the condition to normal at once and completely relieve the pain and discomfort.

In small, localized **abscesses** the use of the fifty-candlepower carbon-filament incandescent therapeutic lamp, at the bedside in houses equipped with electricity, affords a means far more effective than any other method formerly employed, giving great comfort and relief in many painful and otherwise serious conditions. For such purposes it is far superior to the hot-water bag, flaxseed poultices, or other means of applying convective heat, because the effect of radiant energy penetrates deeply into the tissues, producing hyperemia in the deeper structures, whereas the effect of other local applications is, as a rule, confined to the skin.

In cases of **intestinal infection** prolonged applications of radiant light and heat in conjunction with measures employed for the removal of the intestinal contents are the most effective means, affording greater comfort and relief to the patient as well as aiding in restoring the condition to normal.

In **infantile marasmus** and the resulting emaciation the application of radiant light and heat, together with the institution of a suitable routine diet, rapidly overcomes the intestinal

inertia, restoring active function with increased peristalsis of the bowels of the little sufferers. This will be followed in most cases by rapid gain in nutrition and gradual restoration to health. This effect is due largely to stimulation of the general metabolism with increased secretion and functional activity of the intestinal glands and musculature.

In the **constipation of infants**, for the same reason, radiant energy plays a very important part in restoring the evacuations to normal.

It is a remarkable aid in the treatment of **gout**, so-called **rheumatism**, and other toxic or anemic conditions.

In **parenchymatous nephritis** the light bath, when used together with the static wave current, the latter applied over the kidneys, or the direct d'Arsonval current passed through the kidneys, produces results in these cases which are truly remarkable.

In the treatment of **tuberculous affections** radiant light and heat is most effective when employed in connection with other hygienic and physical measures. The most successful routine physical treatment as systematically employed in **tuberculous adenitis** is to employ the X-ray in large doses or, more conservatively, in a series of regulated doses. After the occurrence of a superficial dermatitis or when conditions indicate that the process is in abeyance, the X-ray should be followed by the use of radiant light and heat. In this connection it must be borne in mind that radiant light and the X-ray are antagonists and cannot be administered jointly for therapeutic purposes. This fact was discovered by the writer a number of years since. For this reason we employ the X-ray in a

series conservatively or in a massive dose, to the extent of inducing the physiological effects of inhibition, or until probable sterilization of the germs is effected. The X-ray series is then discontinued and followed by prolonged applications of radiant light and heat.

This general principle of application employed for the treatment of all forms of tuberculosis, either pulmonary or localized, accomplishes remarkable results. Dr. Byron S. Price has reported successful results in **tuberculous peritonitis** by the employment of intense radiant light from high-candlepower tungsten lamps.

Heliotherapy in the treatment of **tuberculous arthritis** in children has proved very efficient. Applied in the open, in the higher altitudes, with the children protected, but the joints fully exposed to the direct rays of the sun, the results after a few months' treatment have been remarkable in the cases published. In **tuberculosis of the kidney**, treatment by the same method has given promising results.

The following description of the general technique of heliotherapy, based on personal study of the methods used in the Rollier clinics, has been given by C. E. Sevier (Jour. Amer. Med. Assoc., Sept. 12, 1925): Before any exposure to the sun, the patient is put to bed at complete rest until accustomed to his new surroundings, change of altitude, temperature, etc.—usually in a few days. After he has been gradually trained to remain in the open air day and night, the body is first exposed to the air, a little more each day, but not to the sun. Two essential principles of the sun bath are strict individualization and careful progression. An average dose of sunlight in the beginning may cause vertigo, headache or nervousness in one patient and simply a feeling of comfort in another. The skin of one patient may burn, while that of another will show no change of color. Dark persons react

more favorably than the fair. Short periods of insolation alternating with periods of rest permit of tolerating more sunlight than one long sun bath. In an average case:

First day: Feet and ankles exposed for 5 minutes 3 times with 10-minute intervals.

Second day: Feet and ankles exposed for 10 minutes, with the legs to the knees for the last 5 minutes; this is done 3 times with 10-minute intervals.

Third day: Feet and ankles exposed for 15 minutes, with the legs for 10 minutes and the thighs for 5 minutes; this is done 3 times with 10-minute intervals.

Next the abdomen and then the thorax are similarly exposed. Thereafter, with increments of 5 minutes, this plan is followed until about the 15th day, after which the entire body is insolated from the beginning of the bath. The maximal exposure is from 3 to 6 hours, according to idiosyncrasies and reactions. When conditions, such as the location or state of healing of the lesion, permit, the patient is turned to the ventral position, and the posterior surface exposed according to the same plan. The head is not exposed and the eyes are protected by smoked glasses.

The principal conditions in which heliotherapy has been shown of special value are: **Tuberculosis of the bones, joints, glands, skin and serous cavities** and, with certain modifications, of the **lungs**; the **acute febrile diseases during convalescence**; **rickets**; the **secondary anemias**; **wounds**, especially when sluggish or with chronically discharging sinuses; **fractures**, particularly with tendency to non-union; **osteomyelitis**, postoperatively; **general debility** without evidences of definite disease; so-called **pre-tuberculous children**. The contraindications are nephritis; high fever with toxemia; advanced circulatory disease; renal tuberculosis when bilateral and with impending uremia. Heliotherapy should be stopped whenever acute intercurrent infection develops.

The sun's rays, while highly toxic to microorganisms in general and the tubercle bacillus in particular, are beneficial to the cells of higher animals. They seem to increase the rate of disintegration of cells damaged beyond repair, while stimulating the undamaged cells. A torpid lesion, such as

varicose ulcer, demonstrates especially well their cicatrizing action. Rollier (*Lancet*, Mar. 19, 1921).

Heliotherapy in **tuberculosis**, when carefully administered with the other therapeutic procedures indicated, is of tremendous value, in a fourfold manner; (1) It acts as a tonic. It has been shown to change the blood picture and probably the blood chemistry in a favorable way. (2) It induces the patient to rest quietly during the exposures. When the latter are long, this becomes an important therapeutic factor. (3) In addition to the sun bath the patient gets an air bath which is of unquestionable value. (4) It is a tangible form of treatment; the patient sees the skin becoming pigmented and feels definitely improved from time to time. Not infrequently, one is enabled to keep a patient on the dietetic and hygienic treatment for months after all treatment would otherwise have been abandoned, thus often securing arrest of the tuberculous process and restoration of working capacity instead of a mere quiescence of the disease. J. A. Myers (*Minn. Med.*, June, 1925).

According to Sajous (*American Therapeutic Society*, June 11, 1926), heat set free by reaction of oxygen with the phosphorus of lecithin causes the enzymes in the tissue cells to digest terminal food-products as well as pathogenic germs and their toxic products. The beneficial effects of heat or light therapy, including heliotherapy and to a certain extent the Röntgen rays, are due to their influence upon this physiologic process. An artificial local fever is thus provoked, emulating Nature's own way of counteracting infection.

In **Addison's disease**, following the Röntgen-ray treatment, light and the d'Arsonval current have proved remarkably helpful.

The antagonistic properties of radiant light and heat to the X-ray were observed by the writer when treating cases of malignant lupus and skin diseases, employing both measures on the same day. The experiment was made under

the impression that the X-ray effect would be accentuated, or at least not impaired; while the light might have some effect in preventing the then universally dreaded dermatitis. In 15 cases of various conditions then under treatment, the experiment being continued for nearly one month, it was found that in every case no progress was made toward improvement. Immediately upon discontinuance of the use of the light in these cases progressive improvement was again observed. It was apparent that radiant light and heat would be the indicated treatment for **acute X-ray dermatitis**, and this has proved uniformly successful, the recovery being prompt in every case except in the chronic X-ray dermatitis of X-ray operators and in cases in which necrosis had already occurred.

The **postoperative use** of radiant light and heat when applied to the surface at the site of the operation is remarkably beneficial, relieving both the pain and the tenderness and at the same time promoting rapid healing. This application may be made without danger by interposing a thin covering of gauze, and continuing the application until an active superficial hyperemia is produced. Such applications will promote prompt restoration of **bruises, incisions, and macerated tissues** and afford marked relief from the **pain and discomfort** present after an operation.

In **postoperative depression with cardiac weakness**, or where some serious internal disturbance has occurred as a result of **shock with lowered vitality** such as may preclude an operation, prompt relief may often be afforded by application of radiant light and heat to the whole trunk of

the body either by means of a high-candlepower incandescent lamp or a properly constructed one-half cylinder tube, 20 to 24 inches in diameter and $3\frac{1}{2}$ to 4 feet in length and provided with numerous incandescent lights arranged in rows so that the radiations will be projected upon the nude body of the patient, the ends being closed to the neck and thighs by sheetings to prevent the escape of the heat. This method in hospital practice, and at the bedside in houses equipped with an ample electric current, may be used also with benefit in the treatment of severe infectious diseases, as **pneumonia** and **typhoid fever**, to combat depression and coincidentally limit the process of infection.

This method is an important one for reviving patients in low states and has proved remarkably effective for the relief of patients suffering from septic infection.

ULTRA-VIOLET RAYS.—These rays are characterized by wave-lengths shorter than the limit of the visible wave-lengths, yet longer than the Roentgen rays. Thus, whereas the visible rays of shortest wave-length (violet) have a wave-length of 3600 Angström units (each unit = one ten-millionth of a millimeter), and the Roentgen rays range from 2 to 12 such units, the ultra-violet rays have a range of 500 to 3600 units.

These rays are secured by means of the mercury vapor lamp, in which an electric current is passed through volatilized mercury. The tube containing the vapor is made of fused rock crystal (quartz), since glass is impervious to rays of wave-lengths shorter than 3022 A. U., and would therefore shut off an important part of the ultra-violet radiation. The electric current used may be obtained from the ordinary street supply, and the apparatus consists essentially of the mercury vapor tube and a box containing a rheostat, a converter where the street current is of the alternating type, and a cooling system where the water-

cooled type of mercury vapor lamp is used. In the air-cooled lamp a mantle of mercury vapor arises around the central luminous stream (owing to the heat liberated) which cuts off the ultra-violet rays of short wave-length. In the water-cooled lamp the mercury mantle is condensed by the cooling device with the result that the rays from such a lamp possess a shorter average wave-length than those from an air-cooled lamp. The rays from the former type are thus stated to be predominantly bactericidal in their effects, chemically reducing, relatively superficial, and depressant to metabolism, while those from the air-cooled lamp are stated to be predominantly biologic in effect, oxidizing, relatively penetrating and synergistic to metabolism.

The ultra-violet rays are not penetrating rays in the sense of the Roentgen rays. With a wave-length of 3000 A. U. the depth of penetration in the skin is said to be 20 microns, and at 2900 A. U., only 2 microns. Bacteria in clear water are, however, killed by ultra-violet rays in a few seconds, and the most highly bactericidal rays are those having a relatively short wave-length of about 2500 A. U. Experiments by Colebrook, Eidinow and Leonard Hill have seemed to indicate that exposure of the skin to ultra-violet radiation gives an increased bactericidal power to the blood and serum. (Heat rays and mustard poultices had the same effect.) This result was referred to improved functions of the leucocytes. Excessive exposures, however, caused an unfavorable effect.

As for the biologic effects of the ultra-violet rays, attention has been particularly drawn to the protection they afford against a lack of antirachitic factors in the diet. It has also been shown that certain foods can be made to acquire antirachitic properties by exposure to ultra-violet rays. These rays also assist in the fixation of calcium where this process is deficient. According to Bierry (C. r. Soc. de biol., Feb. 2, 1926), they act on carbohydrates like a ferment, setting free gases much as do yeasts. A ferment action in the superficial tissues therefore seems a possibility.

The proper dosage of the rays is difficult to state in precise terms, since not only are there variations of individual susceptibility, but many different kinds of instruments are

in use. F. A. Davis (Med. Jour. and Rec., Aug. 19, 1925) begins with an initial exposure of $\frac{1}{2}$ minute to each of 4 body zones (upper and lower and front and back, including the trunk and legs). The eyes are protected by colored goggles, black paper, or gauze or cotton. The average distance of the burner is usually 30 inches. Each treatment is increased by $\frac{1}{2}$ minute to each zone until each zone is receiving 5 minutes. These treatments are given daily, until pigmentation begins to appear, then changed to 3 times weekly and sometimes reduced to 3 minutes to each zone.

The general effects of the ultra-violet rays on respiratory and circulatory diseases are: Intense and persistent hyperemia of the skin; increased appetite, sleep, weight and diuresis; relief of nervous and muscular pains; feeling of renewed vigor, and cessation of night-sweats and fever in tuberculosis. The writer favors the measure in acute bronchitis, pneumonia (all stages), pleurisy (not empyema), asthma, myalgia, thoracic neuralgia, and pulmonary tuberculosis. L. F. Scarpa (Morgagni, Oct. 31, 1921).

In vesicular eczema the ultra-violet rays proved to be soothing and markedly antipruritic. In impetigo and herpes simplex disappearance of pustulation seemed to be hastened. Flat vascular or port-wine nevi and X-ray dermatitis respond well to pressure application of the rays, which constitute by far the most potent agent in these conditions. Some cases of early furuncle were aborted and pain relieved by pressure application. Tuberculous sinuses seemed benefited, and general body exposures appeared to build up resistance. All cases given general exposures showed leucocytosis; therefore, all chronic skin conditions in anemic, undernourished patients are given this treatment. The cases of sycosis coccigenica which respond best are those resistant to X-ray treatment. Beinhauer (Urol. and Cut. Rev., Nov., 1924).

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WILLIAM BENHAM SNOW,
New York.

LIME. See CALCIUM.

LINUM.—*Linum* (linseed or flaxseed) is the dried ripe seed of *Linum usitatissimum*, the common flax. The seeds are oval and flattened. They have no odor, but a mucilaginous taste. They contain a fixed oil, wax, resin, extractive, tannin, gum, mucilage, albumin, gluten, and salts. The fixed oil is found in the interior of the seed, and when expressed without the aid of heat is known as linseed oil (*oleum lini*, U. S. P.). When ground, the seeds form a grayish meal, known as flaxseed meal, ground linseed, or linseed meal. When freshly ground the meal is rich in oil and free from rancidity.

PREPARATIONS AND DOSE.—

Linum, U. S. P. (flaxseed).

Oleum lini, U. S. P. (linseed oil), is a yellowish, oily liquid with a peculiar odor and bland taste, soluble in 10 parts of absolute alcohol, as well as in ether, chloroform, oil of turpentine, etc. Upon exposure to the air it gradually darkens, thickens, and acquires a strong odor and taste. Boiled linseed oil should not be dispensed. Dose, 1 fluidounce (30 c.c.) or less.

Linimentum calcis, U. S. P. (lime liniment; carron oil), is a mixture in equal parts, by volume, of lime water and linseed oil. Used externally.

THERAPEUTICS.—On account of its demulcent action upon mucous membranes, flaxseed has been used in the treatment of bronchitis, gastritis, acute cystitis, and nephritis, frequently in the form of flaxseed tea:—

Flaxseed, 3 drams (12 Gm.).

Extract of licorice, 30 grains (2 Gm.).

Boiling water, 10 ounces (300 c.c.).

Mix, stand in a warm place for three or four hours, and add a little lemon juice or lemon peel, sugar, and 1 to 2 drams (4 to 8 Gm.) of gum arabic. If cough is present paregoric may also be introduced.

Ground flaxseed mixed with boiling water (1 to 2½ parts) forms the well-known flaxseed poultice. It should be spread at least half an inch in thickness upon muslin or flannel, the surface covered with gauze or cheesecloth, and applied as hot as can be borne. It should be covered with thin rubber cloth to retain the heat and moisture and be renewed as soon as it begins to cool or dry. If a counterirritant effect is desired, the surface may be sprinkled with dry mustard or a few drops of turpentine. These applications are useful in pneumonia or pleurisy (as jacket poultice), peritonitis, abscesses, boils, felons, inflamed glands, indolent ulcers, etc. Laudanum may prove a useful addition to a poultice in painful affections.

Carron oil (*linimentum calcis*) is an old and favorite application for excluding air from burns.

Linseed oil, in doses of 1 to 2 ounces, may be used as a laxative and is of especial value when hemorrhoids are present.

W. and S.

LIPURIA.—Normal urine contains slight traces of fatty matters—palmitins and stearin—about 2 grains (0.13 Gm.) per gallon (4.54 liters). Lipuria is physiologic in pregnancy. Roberts has recorded several cases of pure oil in the urine after ingestion of codliver oil. Small quantities of fat have been met with in chronic parenchymatous nephritis, fatty renal changes, acute yellow atrophy of the liver, phosphorus poisoning, diabetes mellitus (often alternating with sugar), hydronephrosis, heart disease, pancreatic disease (oil noted in the urine before its appearance in the stools), after fractures, and in chyluria. Bauman and Hansmann observed a case of progressive nephritis, possibly of syphilitic origin, associated with lipuria and terminating in uremia; the lipuria was influenced by the amount of fat in the diet. Much fat in the urine renders it turbid or milky.

Detection of Fat in Urine.—Under the microscope fatty matter appears in highly-refracting globules of various sizes, with dark margins.

Ether Test.—Shake the urine, add an equal amount of ether, shake again, cork tightly and set aside until the ethereal portion has risen to the top. Pour it off and allow to

cooled type of mercury vapor lamp is used. In the air-cooled lamp a mantle of mercury vapor arises around the central luminous stream (owing to the heat liberated) which cuts off the ultra-violet rays of short wave-length. In the water-cooled lamp the mercury mantle is condensed by the cooling device with the result that the rays from such a lamp possess a shorter average wave-length than those from an air-cooled lamp. The rays from the former type are thus stated to be predominantly bactericidal in their effects, chemically reducing, relatively superficial, and depressant to metabolism, while those from the air-cooled lamp are stated to be predominantly biologic in effect, oxidizing, relatively penetrating and synergistic to metabolism.

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Boiling water, 10 ounces (300 c.c.).

Mix, stand in a warm place for three or four hours, and add a little lemon juice or lemon peel, sugar, and 1 to 2 drams (4 to 8 Gm.) of gum arabic. If cough is present paregoric may also be introduced.

Ground flaxseed mixed with boiling water (1 to 2½ parts) forms the well-known flaxseed poultice. It should be spread at least half an inch in thickness upon muslin or flannel, the surface covered with gauze or cheesecloth, and applied as hot as can be borne. It should be covered with thin rubber cloth to retain the heat and moisture and be renewed as soon as it begins to cool or dry. If a counterirritant effect is desired, the surface may be sprinkled with dry mustard or a few drops of turpentine. These applications are useful in pneumonia or pleurisy (as jacket poultice), peritonitis, abscesses, boils, felons, inflamed glands, indolent ulcers, etc. Laudanum may prove a useful addition to a poultice in painful affections.

Carron oil (*linimentum calcis*) is an old and favorite application for excluding air from burns.

Linseed oil, in doses of 1 to 2 ounces, may be used as a laxative and is of especial value when hemorrhoids are present.

W. and S.

LIPURIA.—Normal urine contains slight traces of fatty matters—palmitins and stearin—about 2 grains (0.13 Gm.) per gallon (4.54 liters). Lipuria is physiologic in pregnancy. Roberts has recorded several cases of pure oil in the urine after ingestion of codliver oil. Small quantities of fat have been met with in chronic parenchymatous nephritis, fatty renal changes, acute yellow atrophy of the liver, phosphorus poisoning, diabetes mellitus (often alternating with sugar), hydronephrosis, heart disease, pancreatic disease (oil noted in the urine before its appearance in the stools), after fractures, and in chyluria. Bauman and Hansmann observed a case of progressive nephritis, possibly of syphilitic origin, associated with lipuria and terminating in uremia; the lipuria was influenced by the amount of fat in the diet. Much fat in the urine renders it turbid or milky.

Detection of Fat in Urine.—Under the microscope fatty matter appears in highly-refracting globules of various sizes, with dark margins.

Ether Test.—Shake the urine, add an equal amount of ether, shake again, cork tightly and set aside until the ethereal portion has risen to the top. Pour it off and allow to

evaporate. The residue will show if fat or oil is present. Fat in a milky, opaque urine points strongly to chyluria.

LITHEMIA (uricacidemia; uricacidosis) is a condition in which, owing to defective metabolism of the nitrogenous elements, the blood becomes charged with deleterious substances, chiefly of the uric acid group.

SYMPTOMS.—The symptoms are manifold, but may be grouped as follows: 1. Nervous symptoms: headache, paroxysmal or periodic; neuralgic pains in the bones or joints, cerebral excitement, insomnia, convulsions, and neurasthenia. 2. Digestive disorders: cyclic vomiting, colic, polyphagia, constipation, membranous enteritis, and intestinal lithiasis. 3. Urinary troubles: renal calculus and colic, albuminuria, glycosuria, dysuria, cystitis, and spasm of the bladder. 4. Respiratory ailments: coryza, sneezing, laryngitis, bronchitis, asthma, and pulmonary congestion. 5. Circulatory derangements: palpitation, tachycardia, arrhythmia, false hypertrophy, and myocardial symptoms without any lesion of the myocardium. 6. Cutaneous affections: eczema, sweating, and pruriginous eruption. 7. Various pathological disorders of the eye, ear, nose, and throat.

DIAGNOSIS.—A careful study should be made of the patient's ability to metabolize the various food elements, especially the nitrogenous and the purin-forming foodstuffs (nucleoproteids—meat, fish, fowl, eggs, peas, beans, lentils, etc.) A thorough analysis will, moreover, generally lead to correct conclusions, or at least suggest further investigations, and thereby establish the diagnosis.

ETIOLOGY AND PATHOLOGY.—Heredity is an important factor in the etiology of the condition, and may exhibit itself in inactive liver or kidneys, incapable of adapting themselves to a particular mode of life; a digestive apparatus that, while it tolerates a surplus of food, is unable completely to metabolize it; an irritable sympathetic nervous system which responds excessively to slight disturbing causes. A morbid desire for proteins and the purin-forming foods overtaxes the normal metabolism, and the uric acid toxemia thus brought about causes a contraction of

the arterioles, and a diminished capillary circulation results; the blood-pressure rises and, where the vessel walls are either intrinsically weakest or relatively weakest because of less support from extravascular tissue, engorgement must occur. Stasis added to this produces inflammation.

TREATMENT.—In the line of prophylaxis thorough mastication should be enjoined. The robust, plethoric patient should take regular outdoor exercise with the idea of consuming his body-fats. Horseback riding, rowing, golf, and walking are suggested. The nervous patient, on the other hand, needs rest and quiet. The constant use of lithia water has been advocated.

Assuming that certain cases are produced by an autointoxication from the alimentary tract, and with the object of limiting fermentation, Anders recommends a diet consisting chiefly of proteins, combined with the free use of water. When the gastric digestion is poor, carbohydrates will agree better. Cream and butter are the only forms of fat allowed, and the use of alcohol is forbidden.

The medicinal treatment is that used in gout, to which the reader is referred. To aid the digestion of the proteins, hydrochloric acid may be indicated; if the appetite is impaired a simple bitter or *nux vomica* may be combined with the acid. W.

LITHIUM.—Lithium is one of the alkali metals, and is generally derived from lepidolite, a native silicate. It occurs in minute quantities in some mineral springs. The metal is not used in medicine, but some of its salts are semi-official.

PREPARATIONS AND DOSE.—*Lithii benzoas*, N. F. (lithium benzoate) [$\text{LiC}_7\text{H}_5\text{O}_2$], occurs as a light, white powder or small crystalline scales, odorless, stable in the air, and with a cooling, sweetish taste; it is soluble in 3 parts of water and in 13 parts of alcohol. Dose, 5 to 20 grains (0.3 to 1.3 Gm.).

Lithii bromidum, N. F. (lithium bromide) [LiBr], occurs as a white, granular salt, with a sharp, slightly bitter taste, very deliquescent, soluble in 0.6 part of water, and also freely soluble in alcohol. Dose, 5 to 20 grains (0.3 to 1.3 Gm.).

Lithii carbonas, N. F. (lithium carbonate)

[Li_2CO_3], occurs as a light, white powder, with an alkaline taste, soluble in 78 parts of water, more soluble in water saturated with carbon dioxide, insoluble in alcohol, but soluble in diluted acids with effervescence. Dose, 3 to 10 grains (0.2 to 0.65 Gm.).

Lithii citras, N. F. (lithium citrate) [$\text{Li}_3\text{C}_6\text{H}_5\text{O}_7 \cdot 4\text{H}_2\text{O}$], occurs in a white powder or in granular form, with a cooling, slightly alkaline taste, deliquescent in moist air, soluble in 1.4 parts of water, but practically insoluble in alcohol. Dose, 3 to 10 grains (0.2 to 0.65 Gm.).

Lithii salicylas, N. F. (lithium salicylate) [$\text{LiC}_7\text{H}_5\text{O}_3$], occurs as a whitish powder, with a sweetish taste, deliquescent in moist air, and very soluble in water and alcohol. Dose, 5 to 20 grains (0.3 to 1.3 Gm.).

PHYSIOLOGICAL ACTION.—Lithium carbonate and citrate, used in medicinal doses, act partly as lithium and partly as alkalinizers; the benzoate, bromide, and salicylate of lithium, on the other hand, are employed chiefly for the action of their acid constituents.

Binet has shown that lithium salts in large doses give rise in animals to the following series of symptoms: weakness, diarrhea, nausea, dyspnea, fall of temperature, convulsions, and death. The last is attributed to depression and final arrest of the heart in diastole, coupled with depression of the respiratory centers. The peripheral nervous system is paralyzed and muscular excitability reduced by lithium.

Lithium salts, after absorption, are excreted in the saliva, into the stomach and bowel, and in the urine.

Experiments have shown that lithium in large doses has the special property of causing gastroenteritis, which results even if the salt be given subcutaneously.

UNTOWARD EFFECTS AND POISONING.—Lithium carbonate, in 15- to 20-grain (1 to 1.3 Gm.) doses, and lithia tablets have been known to cause gastrointestinal symptoms in man. Cleaveland, after taking rather large doses (30 grains—2 Gm.) of lithium chloride, experienced toxic symptoms when a total of 125 grains (8 Gm.) had been ingested during twenty-eight hours. There followed marked muscular and general prostration, vertigo, and eye and ear symptoms resembling those

of cinchonism. There was complete absence of gastrointestinal symptoms. Two or 3 doses (60 to 90 grains—4 to 6 Gm.) daily were sufficient to cause the toxic phenomena.

THERAPEUTICS.—The preparations of lithium at one time held a high reputation for efficiency in the treatment of the so-called "uric acid diathesis." It was claimed that they could dissolve uric acid calculi in the urinary passages or in the bladder. Haig called attention, however, to the fact that, although lithium forms a relative soluble salt with uric acid in the test-tube, in the body it has a greater affinity for the acid sodium phosphate in the blood, the uric acid being thus left uncombined. Besides, the relatively high solubility of lithium urate has been shown to hold good only in concentrated solutions, and not to be available in solutions such as can be used in the body (Sollmann).

The carbonate, citrate, and salicylate of lithium are being gradually less used in the treatment of **rheumatoid arthritis**, **gout**, and **subacute** and **chronic rheumatism**. The carbonate is but moderately soluble in water (1 to 75), and is sometimes given in freshly made pills or capsules. The citrate may be given in solution alone, in Vichy water, or in combination with other remedies. Lithium citrate, $1\frac{1}{2}$ drams (6 Gm.) dissolved in 2 ounces (60 c.c.) each of spirit of Mindererus and syrup of lemon, may be given in dessertspoonful doses every two or three hours in **rheumatism** or **gout**. Lithium salicylate, 10 to 20 grains (0.65 to 1.3 Gm.) every three hours, has been considered especially useful in subacute rheumatism.

The lithium salts have been given in **cystitis** and **gravel** with asserted benefit. If there is an increased secretion of ropy mucus and the urine is alkaline, lithium benzoate is to be preferred, since it renders the urine more acid; when the urine is already too acid, the carbonate or the citrate should be used.

Lithium bromide has been employed for the effect of the bromine it contains, *e.g.*, in **epilepsy**. Its hypnotic power was regarded by Weir Mitchell as superior to that of potassium bromide. W. and S.

LIVER AND GALL-BLADDER, DISEASES OF THE.

DISEASES OF THE LIVER.

MALFORMATIONS.—Abnormalities in the form of the liver may be either acquired or congenital.

1. Corset Liver.—The constant pressure of the lower ribs against the liver as a result of tight lacing or the wearing of a tight waist-band may produce a deep, transverse furrow on the right lobe. The furrow usually corresponds to the margin of the ribs, and may be so deep that the liver becomes divided into a large upper and a small, lower, part connected by a narrow isthmus or band composed chiefly of fibrous tissue, the larger blood-vessels, and bile-ducts. The peritoneum in the groove is much thickened. The lower portion is usually rounded and may be freely movable as if hinged to the upper, and appear in the abdomen as a movable tumor.

This deformity is met with usually in elderly females. There are usually no symptoms resulting from the deformity; yet in some there is said to be a constant sensation of pressure and weight in the hepatic region. In occasional cases, owing to venous stasis, there is a temporary swelling of the isolated portion and violent pain and signs of irritation of the peritoneum.

The so-called **Oriental constricted liver** is attributed by Oshima (Sei-I-Kwai, Mar. 20, 1919) to the pressure exerted by the Japanese woman's belt, aggravated by the low sitting posture. EDITORS.

2. Tongue-like Lobes.—These are probably of much more frequent occurrence, and therefore of much more importance, than the corset liver. They are both of importance chiefly on account of the difficulties they present in diagnosis. Riedel met with 12 cases

of tongue-like lobes in 42 operations for gall-stones. I have met with 9 in various conditions. In 2 the mass was thought to be a movable kidney, and in 1, an infant with hemorrhagic pancreatitis, it was thought that possibly the tongue-like lobe was an intussusception. They are met with at all ages, and are probably usually congenital rather than acquired from external pressure. The diagnosis of these malformations is usually easy if the abdominal wall is thin and lax, as the connection of the mass with the liver can be definitely traced; but if the abdominal wall is thick from the deposit of fat or its muscles tense it is often impossible to differentiate these from other masses met with in the abdomen. An effort should be made to outline the mass and trace its connection with the liver. This is often impossible, as the base may be deeply furrowed and a loop of intestine may occupy the groove.

Treatment for these abnormalities is rarely called for. When the mass is troublesome from its mobility, and cannot be retained by a suitable bandage, it may be removed. Such has been done successfully.

The chief interest in this subject is in connection with the diagnosis of abdominal tumors. Unless fully alive to the great variety, as to shape and position, in which these accessory lobes of the liver may present themselves, one will often be misled in the diagnosis of abdominal tumors. In not a few cases, even with the utmost care, a positive opinion as to the nature of these tumors cannot be given.

Riedel, who first drew attention to the importance of these abnormal lobes, believes them to be due usually to pressure on the liver, as in tight lac-

ing, and to traction, by an enlarged gall-bladder. They are met with usually in women. In 9 of his 12 cases the gall-bladder was attached to the lower part of the process.

So far as can be inferred from the 9 cases which I have met, tight lacing has little to do with the production of the deformity, and the position of the gall-bladder at the lower part of the mass is an accident rather than a cause of its formation. In many, if not almost all, cases the formation of these lobes seems to be developmental, having nothing to do with either pressure or traction.

DISPLACEMENTS. — Displacements of the liver may be either congenital or acquired. As instances of the former are hernia of the liver through the diaphragm and through the anterior abdominal wall. Interesting examples are also afforded by transposition of viscera, the liver being found to the left and the spleen to the right. As a rule, the other organs, both of the thorax and abdomen, are also transposed, the cardiac impulse being in the fourth or fifth intercostal space to the right; but the liver and spleen may be the only organs abnormally placed.

There may be no symptoms, the condition being discovered accidentally. On the other hand, they may be severe, consisting of pain, tension, and dragging sensation in the normal hepatic region. Jaundice, sometimes severe, has been present in a few cases, probably due to tension or kinking of the common bile-duct. Hypochondriasis is apt to develop. The diagnosis may be difficult. Other masses—as carcinoma of the omentum, tumors of the right kidney, etc.—have been supposed to be mov-

able liver. Of the greatest diagnostic importance are the form of the tumor, its mobility, the possibility of reducing it to its normal position, the tympanitic note obtainable over the normal hepatic region before such reduction, and the dull note later.

Etiology.—Acquired displacements may be due to pressure upward by ascitic effusion, abdominal tumors, and flatulent distention, and downward by thoracic or subdiaphragmatic accumulations. These are, however, scarcely entitled to be included among liver displacements. The movable or wandering liver is of more interest. The condition is not very rare.

Graham, who studied 66 cases, concluded that displacement was found chiefly in females who have borne several children. The displacement is favored by a lax abdomen, tight lacing of the lower part of the chest, and sudden muscular strain. To render these causes effective it is probably necessary that the ligaments supporting the liver be abnormally long or weak: a condition that is doubtless congenital.

Treatment.—Treatment is not very satisfactory. A suitable **bandage** may relieve symptoms. The liver cannot be retained in the normal position by it, but further prolapse may be prevented and the liver so far supported as to relieve the pain and dragging. In a few cases the liver has been successfully sutured in position (**hepatopexy**).

General massage and lipotherapy, which have for their aim the strengthening of the organism, are of high value, according to Einhorn. In the front rank of all these methods is **diet rich in butter**. The patient should be directed to take as

much food as other healthy persons, and a little more. To the ordinary diet Einhorn adds $\frac{1}{4}$ pound of butter daily to increase weight. **Gymnastic exercises in the open air**, and, in cases with tendency to constipation, **special exercises for the abdominal muscles**, are likewise of value.

Less commonly present than, but equally as important as, Riedel's lobe is the "floating lobe," a detached portion found appended to the left extremity of the liver by a fold of peritoneum containing blood vessels. Such floating lobules rarely produce symptoms, but can yield definite signs, simulating tumors or an accessory spleen. In a case of Inglis' the additional liver lobe formed a pulsatile and expansile tumor. The writer's case was in an obese female of 86, with chronic mental disease. A mass of hepatic tissue the size of a hen's egg was attached to the left edge of the liver by a double fold of peritoneum. A. J. E. Cave (Lancet, Feb. 13, 1926).

CONGESTION OF THE LIVER.

This pathological condition does not constitute a disease of itself, but is always associated with disease elsewhere, especially of the gastrointestinal tract and of the heart. The liver is particularly prone to disturbance of its circulation, because, in the first place, of its large blood-supply and, in the second place, on account of its relationship to the gastrointestinal tract on the one side and to the heart on the other. As the bulk of its blood-supply is conveyed to it by the portal vein, it will share in all the congestive disturbances of the organs drained by the portal system. The increased *inflow* of blood resulting from these disturbances constitutes an active congestion of the liver. On the other side its proximity to the heart, and the absence of valvular

structures between it and the heart render it very susceptible to any obstruction at the tricuspid orifice. Such conditions offer an impediment to the *outflow* of blood from the hepatic veins, and result in passive congestion of the liver.

Functional derangement of the liver is frequent and generally secondary to a disturbance in some other part of the organism. One of the best criteria is the presence of an increase in the vertical area of liver dullness which declines or disappears as the result of treatment. The symptoms may be enumerated thus: Coated tongue, a bitter taste in the mouth, nausea, a perverted appetite, flatulence, constipation with clay-colored stools, sallow complexion, irritable skin, dull headaches, mental depression, lassitude, insomnia, irritability of temper, drowsiness after eating, a disinclination for work, sense of weight or discomfort in the right hypochondrium, and occasionally an ache in the tip of the right shoulder. The writer believes that the chief causes of this condition of liver derangement are: Dyspepsia, gastrointestinal disturbance, alcoholic excess, rich and highly seasoned foods, fevers, nervous influences, and residence in the tropics. Bain (Brit. Med. Jour., May 18, 1912).

ACTIVE CONGESTION.—The symptoms of acute congestion of the liver are those of gastrointestinal catarrh, such as headache, malaise, foul taste, coated tongue, constipation, etc. With these may be present a sense of discomfort, weight, or even pain in the region of the liver, which may also be tender on pressure. The liver may be felt below the costal margin. There may be slight jaundice; in the severe tonic cases the jaundice may be intense.

Two cases of severe pain back of the sternum and in the upper abdo-

men due to acute congestion of the liver, greatly aggravated after climbing a hill. During the attack the liver was found extremely enlarged, reaching from the fifth intercostal space to the umbilicus, the mechanical conditions amply explaining the pain back of the sternum. The urine was concentrated, with considerable urobilin. The same clinical picture was soon presented by a third patient; the paroxysmal attack following the hill-climbing test was so severe that the patient went to bed without returning to report at the physician's office. The whole trouble was evidently extremely severe acute congestion of the liver, and the writer thinks that this is a wise effort on the part of nature to relieve the strain on the weak right heart from the physical exertion. Nature drives the blood into the liver and relieves conditions in the heart as from a venesection, giving the heart a chance to recover. Ortnier (Med. Klinik, Sept. 21, 1913).

The urine is dark, heavy, somewhat scanty, and loaded with urates.

Diagnosis.—The diagnosis is based on the association of the symptoms of gastrointestinal disturbance, with the enlargement of the liver, besides the discomfort in the hepatic region.

Acute hepatic congestion is very common in nurslings, and not rare in older children. It may be caused by overfeeding and is often observed after trips to the mountains, seashore, etc., which excite the appetite beyond the digestive powers of the child. The stools are deficient in bile, pale and fetid, the urine dark, the liver tender and the temperature more or less raised. Raimondi (Presse Médicale, Nov. 19, 1917).

Etiology.—There are two main groups of causes: (1) gastrointestinal and (2) toxic. The most common of the first are catarrhal conditions of the stomach and intestines resulting from undue indulgence in

food, and drink, especially if of a stimulating nature, as spices and alcohol. The habitual use of spirits to excess furnishes the most marked examples in these northern climates. Persons of sedentary habits are more liable to be affected, especially at middle age. Toxic causes occur in infectious diseases, especially in malaria, dysentery, typhoid fever, yellow fever, etc. Even these causes act chiefly through the gastrointestinal tract. They are much more common in tropical climates.

Active congestion of the liver is also met with in suppressed menstruation and in diabetes mellitus. In both of these it has been attributed to vasomotor disturbance, but in diabetes the increased work thrown on the liver may be the chief cause.

Morbid Anatomy.—The liver is enlarged, dark in color and the vessels full of blood. The distention of the lobule with blood is not limited to the center, but is general. There is often some fatty change in the liver-cells.

Treatment.—The indications are chiefly two: (1) to correct the habits that have mainly caused the condition and (2) to relieve the gastrointestinal condition and the hyperemia of the liver. We aim at attaining both objects simultaneously. The diet should be of the blandest nature. In severe cases no food should be given until the bowels are acted on and the portal system depleted by a brisk laxative. Water should be taken freely on an empty stomach. The food should be regulated according to the needs of each case so as not to tax the digestive powers. Exercise should be free, but without undue fatigue.

Where hepatic congestion is the result of heart disease the first indication is to lower the venous blood-pressure by **venesection**, **wet cupping**, or by drastic or saline **cathartics**. For the first six to twenty-four hours, according to the intensity of the symptoms, only **boiled water** should be given, then **milk** diluted with boiled water, and finally milk alone, to the amount of 1½ liters (quarts) a day, gradually increased to 2½ liters. The administration of **digitalis** is started at the same time. Diuresis may be continued with doses of 7½ grains (0.5 Gm.) of **theobromine** three times a day. Copious **intestinal irrigations** with cold boiled water, **alkalies**, **saline purgatives**, **cholagogues** in small doses, and **tub baths** followed by **massage** of the whole body may be given. Where there is cardiac enlargement **digitalis** may be replaced by the following combination:—

℞ *Ext. ergotæ*,
Pulv. scillæ,
 āā gr. iss (0.1 Gm.).
Hydrarg. chlo-
ridi mitis gr. ¾ (0.048 Gm.).
Pulv. digitalis . gr. ⅜ (0.024 Gm.).
 M. et ft. pil. no. j. Ft. tal. no. xxv.
 Sig.: One pill three times a day.

Vires (Jour. des prat., Mar. 6, 1912).

According to Lutz, an occasional **transduodenal lavage** with 1 liter (quart) of **hypertonic salt solution** or a **saline cathartic** is beneficial. **Ammonium chloride**, 20 grains (1.3 Gm.) 3 times daily, may prevent congestion and stimulate elimination of wastes. At first it may be used with **alkalies** and later with **nitrohydrochloric acid**, **nux vomica**, and a **bitter tonic**.

Raymond and Duchesne have recommended **douching over the liver**, preceded by a general warm shower. A movable spray is played over the liver until the skin is red, then a cold jet for 10 to 30 seconds.

PASSIVE CONGESTION OF THE LIVER.—Passive congestion of the liver (*nutmeg liver*, *cardiac liver*,

red or cyanotic atrophy of the liver), is a pathologic condition caused by obstruction to the outflow of hepatic blood.

Symptoms.—The symptoms are chiefly those of the condition of the heart and lungs causing the hepatic congestion. There may be a sense of weight and fullness in the right hypochondrium, aggravated by external pressure, deep inspiration, and by lying on the left side.

Enlargement of the liver is one of the chief signs and is usually best demonstrated by palpation. When large, the liver can often be delimited by inspection. Percussion is usually unreliable on account of distention of the intestines.

Pulsation of the liver is often present in severe cases; it disappears when the induration develops and the heart becomes weak. I have seen it persist in cases of initial stenosis until within a few weeks of death.

Gastrointestinal symptoms are always present. They result from the portal congestion induced by the hepatic obstruction. They consist in disturbed digestion, and, often, hemorrhoids.

Ascites is frequent. In the early stage it occurs as a part of general dropsy. Later, when the liver becomes indurated it is increased by the portal obstruction. Jaundice is usually present, and is a definite symptom in the advanced cases. It is probably secondary to the gastroduodenal catarrh. It is usually most marked in the cardiac cases, and, with the cyanosis existing in such cases, it causes a peculiar dusky green tint.

The urine shows high specific gravity and is scanty.

Etiology.—The causes leading to this condition are such as lead to inter-

ference with the free flow of blood through the heart, and include, therefore, all changes in the heart and lungs which tend to render the right ventricle incompetent. Of the cardiac conditions the most common is mitral disease, especially stenosis; but all heart-lesions, whether of the valves or of the substance of the heart, tend to impede the venous flow by ultimately overtaxing the right heart. Such diseases of the lungs as emphysema, asthma, chronic bronchitis, etc., are also frequent causes of dilatation of the right heart, and thus lead to obstruction to the hepatic outflow.

Deformity of the spine, pleuritic effusion, aneurism, and intrathoracic tumors may obstruct the flow of blood through the heart and lungs or press upon the vena cava directly.

Occasionally a local lesion, as peri-hepatitis, may compress the hepatic veins themselves or the vena cava and obstruct the outflow from the liver.

Morbid Anatomy.—In the early stage there is great engorgement of the hepatic veins and their intralobular branches and capillaries. The liver may become much enlarged, its lower border extending in time to, or even below, the umbilicus. If the obstruction be removed before organic changes have occurred in the liver, the vessels rapidly empty themselves, and the liver returns to its normal size. Even after long-continued congestion the liver may be much smaller after death, unless escape of the blood from the hepatic veins is prevented by distention of the right ventricle.

Persistent hyperemia leads in time to structural changes. As the intralobular veins are greatly dilated, the liver cells around them atrophy from pressure,

and blood-pigment is deposited. The center of the lobule becomes dark, contrasting strongly with the periphery, which becomes yellowish, on account of fatty degeneration of its cells; hence the "nutmeg" appearance of the section of tissue.

A careful histological study showed that passive congestion of the liver occurred in five different types: (1) Capillary dilatation with atrophy of central cells, found in moderate circulatory disturbances of various kinds; (2) central degeneration with or without congestion, a stage of degeneration slightly more advanced than the preceding; (3) central fat accumulation with hyperemia or necrosis, a peculiar type usually found in the young in acute rheumatic fever; (4) central necrosis usually associated with hemorrhage, the advanced nutmeg lesion described by Mallory; (5) collapse fibrosis or cardiac cirrhosis. This last condition is more apparent than real, there being little if any increase in the amount of connective tissue originally possessed by the liver. The important factors which lead to the various changes in the liver substance are blood stasis, tissue asphyxia, interstitial hemorrhage and autolysis. The actual effect of the blood-pressure upon surrounding tissues appears to be slight. Lambert and Allison (*Bulletin Johns Hopkins Hosp.*, Dec., 1916).

In course of time atrophy of the liver cells is succeeded by increase of connective tissue. Shrinking and induration result, and may lead to considerable reduction in the size of the liver.

Treatment.—The treatment is chiefly that of the condition of the heart or lungs that causes it, at the same time endeavoring to relieve portal congestion. The latter is usually effected by the action of cathartics. A more rapid effect may be

obtained by local depletion with **leeches**, 5 or 6 being applied over the liver. Their application is usually attended by marked relief when there is pain and distress in this region.

Rest is an important feature of the treatment owing to the decreased heart action that attends it.

Calomel, in repeated doses, is not only an active cathartic, but also an efficient diuretic in such cases. **Digitalis** may be combined with it to increase the power of the heart and secure greater diuretic effect. The condition of the heart requires the administration of heart-tonics, as **digitalis**, **strychnine**, etc. Vegetable cathartics—as **podophyllin**, **colocynth**, **jalap**, **aloes**, etc.—may be used, or salines, such as **sulphate of soda**, **sulphate of magnesia**, or the natural purgative waters (such as **Apenta** or **Hunyadi**, **Rubinat**, **Hawthorn**, **Friedrichshall**), etc.

A combination of **sodium salicylate** and **sodium benzoate** is useful as cholagogue and for “flushing-out” effects in various disorders. Sodium salicylate induces flow of concentrated bile; sodium benzoate, of dilute bile. Relative amounts of two salts to be varied according to indications. Formula suggested: **Sodium benzoate**, 0.75 Gm. (12 grains); **sodium salicylate**, 0.5 Gm. (8 grains); **sodium borate**, 0.25 Gm. (4 grains); **rhubarb**, 0.3 Gm. (5 grains); to be taken *t. i. d.* **Polain-Cartier** (*Revue de therap.*, Oct. 1, 1911).

PERIHEPATITIS.—This consists in an inflammation of the peritoneal capsule of the liver. Inflammation of the fibrous capsule apart from the peritoneal occurs only as secondary to interstitial hepatitis.

Inflammation of the peritoneal covering of the liver may occur either as a part of general peritonitis or as

a local disease. It may be acute or chronic, the former being usually suppurative while the latter is always fibrinous or adhesive.

ACUTE PERIHEPATITIS; SUBPHRENIC ABSCESS; PYOPNEUMOPERIHEPATITIS.—**Symptoms**.—The development of the disease may be with striking symptoms suggestive of perforative peritonitis of the upper part of the abdomen, or it may be so insidious as not to attract attention until the abscess has attained a large size.

Pain in the right hypochondrium or epigastrium is the most prominent symptom. It is increased by pressure and movement; hence the respiration is shallow and costal. Fever, often ushered in by a chill, is present; it may be quite remittent. There may also be abdominal distension, vomiting, hiccough, slight jaundice, weak pulse, etc.

A history of recent appendicitis or liver trouble may give the clue when there are no local subjective or objective signs of the abscess, the general condition does not improve as rapidly as anticipated, and fever drags along after the primary affection is supposedly conquered. Only rarely is subphrenic abscess ushered in with a chill, high fever, and pain. In the subacute cases there may be pain in the intercostal spaces or below the costal arch; the side involved does not share in the breathing excursions as much as usual. Percussion reveals a zone of relative dullness which in front has a cupola-like outline. The liver seems to be pushed down, the heart up. Accumulation of gas in the region is revealed by resonance between the lung and liver, changing its location as the patient changes position. Röntgenoscopy shows the diaphragm abnormally high, and reveals accumulation of gas, but if the pleura is involved the röntgenoscopic find-

ings may be misleading. If exploratory puncture brings pus, the indications for operative treatment are given at once. By introducing and withdrawing the cannula very slowly, there is less danger of missing the abscess; it may be necessary to puncture at several points before the pus is discovered. The writer is confident that if the space just below the diaphragm is examined more as a routine measure, the findings will clear up many puzzling cases and suggest effectual treatment. He reports several cases from his own experience in which the subphrenic abscess developed after operative treatment of perforation of a gastric or duodenal ulcer. In the majority of cases the appendix was the primary seat of trouble. In differentiating subphrenic abscess, empyema, pyopneumothorax, pulmonary and hepatic abscess, and echinococcus cyst of the liver are the affections which have to be excluded. G. Ledderhose (*Deut. med. Woch.*, July 31, 1913).

The physical signs presented will depend largely on the size of the abscess. In the beginning there may be a friction rub. If the abscess is large there is presented great fullness in the right hypochondrium, with extension upward of hepatic dullness, even to the angle of the scapula, and of the edge of liver downward, it may be, to the umbilicus. The upper limit of dullness is convex toward the thorax, following the curve of the diaphragm. Over this area there is absence of all respiratory signs. The course of acute perihepatitis, in the absence of suppuration, may be rapid, recovery taking place in a few days; in suppurative cases it may be prolonged for months, with all the symptoms of chronic suppuration, as irregular temperature, sweats, loss of flesh, etc. In many cases fistulous openings take place through the dia-

phragm, causing a localized empyema, which, in time, perforates the lung into a bronchus, with abundant purulent expectoration, or externally through an intercostal space. In others the abscess discharges into the stomach or intestine. The general course of subphrenic abscess resembles that of empyema or abscess of the liver. The result is usually fatal, unless drainage be established. According to Sonnenberg, the mortality of unoperated cases is 55.5 per cent.; according to Elsberg, 82 per cent.

Diagnosis.—In subphrenic abscess the signs are so indefinite that a diagnosis is often difficult to make. The abscess is usually mistaken for empyema. A history of disease of the stomach, duodenum, or gall-bladder would indicate a perihepatitis, as would also a history of abscess from appendicitis. The absence of a history of intrathoracic symptoms—such as cough, expectoration, etc.—renders pleuritic disease improbable.

The physical signs are those of massive enlargement of the liver; if the abscess cavity contains air, the signs of movable dullness and tympany of pneumothorax are added. However, the bulging of the right side is greater below the diaphragm rather than above. The diaphragm may be pressed upward to the third, or even the second rib, but, however high it is, its limits are well defined and above it the respiratory sounds are not obscured. The lower border of the liver may be greatly depressed. The heart is not as much displaced as it is in pleural effusion.

Usually when the abscess is secondary, and frequently when it is primary, it is mistaken for a condition

above the diaphragm. The typical physical signs are dullness or flatness, diminished breath and voice sounds and vocal fremitus, with râles over the base of the lung. The dullness is convex upward and does not change with change of position. If gas is present there are 3 zones of different resonance: Normal above; below this, tympany, and lower still, flatness caused by the pus and which is continuous with the liver dullness on the right side. Frequently, however, the signs are very confusing. The abscess may be so well walled off that there is little absorption and therefore only a slight increase in the temperature or the leucocyte count. J. Douglas (*Ann. of Surg.*, June, 1924).

On exploratory puncture, if the pus is reached, the spurting is most forcible on inspiration, owing to the descent of the diaphragm. This would practically be conclusive evidence of the seat of the abscess. The presence of bile pigment in the pus would also indicate that the abscess is below the diaphragm.

Fluoroscopy may be helpful, and should be carried out carefully before exploratory puncture is resorted to.

The leucocyte count differentiates hyperemia of the liver from amebic abscess, according to the writer, as shown in 22 cases. When there is actual suppuration there is increasing leucocytosis but no eosinophils and scanty lymphocytes. The mononuclears decrease while the neutrophils increase. There is considerable shifting to the left in the Arneht scale. All these changes are progressive. In mere hyperemia, reverse conditions prevail and remain stationary. Neeb (*Mededeel. d. Burg. Geneesk. Dienst*, 2, 1920).

In 3 out of the author's 9 cases sub-diaphragmatic abscess followed an appendectomy. Four cases died. Stress laid on the value of X-ray examination in the diagnosis, and on the influence of early diagnosis on the outcome.

The X-ray evidences consist of elevation of the diaphragm, accentuation of its dome and limitation of its excursions. There may also be visible a collection of gas beneath it. The procedure almost invariably gives definite information, and promiscuous needling for diagnosis is never indicated. F. M. Hodges (*Jour. Amer. Med. Assoc.*, Apr. 14, 1923).

For early diagnosis, accurate clinical observation is far more important than the X-ray, which gave repeatedly negative results in 1 of the author's cases. In the few cases in which a diagnosis cannot be reached clinically, an exploratory aspiration, as advocated by Beck, is required. The needle is inserted in the posterior axillary line opposite the first lumbar spinous process and introduced upward and backward, in various directions, at an angle of less than 45 degrees. L. Nather and E. W. A. Ochsner (*Surg., Gyn. and Obst.*, Nov., 1923).

Etiology.—It occurs occasionally from a blow or direct injury. It is usually secondary to disease in some adjacent part of the liver itself, such as: Perforating ulcer of the stomach or duodenum, perforation of the gall-bladder, perforation of the intestine or the appendix; abscess of, or in the region of, the kidney, spleen, or appendix; suppuration in the right pleura, the pyogenic organisms making their way through the diaphragm by the lymphatics; abscess of the liver, echinococcus cyst of the liver, suppurative cholangitis, etc., general peritonitis, and traumatism.

Analysis of 76 cases by Barnard showed that about one-third of them were due to perforating gastric and duodenal ulcers. In the majority of the cases due to gastric ulcer the perforation was on the anterior wall of the stomach and near the lesser curve. The septic matter escaped directly into the left anterior intraperitoneal space and the abscess was localized there. About one-sixth were due to appendicitis.

In 2 of the writer's 4 cases the only apparent source of the condition lay in furuncles which had run their course a few weeks before the initial symptoms of the abscess. In another there had been a lung infection, presumably bronchopneumonia, while in the fourth a definite cause for the abscess was discovered, *viz.*, a ureteral calculus with pyonephrosis. Prompt recovery followed evacuation of the abscess in each case. B. Akerblom (Acta med. scand., Jan. 24, 1924).

Morbid Anatomy.—In the early stage the peritoneum of the liver and of the corresponding part of the diaphragm presents the signs of inflammation. The inflammation at the margins of the affected area being less severe, adhesion of the opposing surfaces takes place, while the exudate in the central part, being rich in leucocytes, liquefies, and an abscess results. The abscess may be small or so large as to contain a quart or more of pus. The pus may be creamy and odorless, but more often it is fetid and contains necrotic tissue. It may be dark red from admixture of blood or green from bile. Sometimes air or gas is present, even when no communication with a bronchus or with the stomach or bowel can be found. These abscesses are found usually between the right lobe of the liver and the diaphragm, but may be over the left lobe.

Treatment.—In the early stages the aim of treatment should be to secure relief from pain and arrest of the inflammation. This is best effected by **rest in bed**, the application of 5 or 6 **leeches** over the seat of disease, and, if necessary, the hypodermic injection of **morphine**. Purging freely by **salines** may be of much benefit. Useful, but less effective, means than leeching are the local application of

heat, poultices, sinapisms, or blisters. **Strapping** and the **ice-bag** are also available measures. As soon as the formation of pus can be determined, **free drainage** should be resorted to. This may necessitate the **resection** of one or more ribs, but in any case the drainage should be as complete as possible.

In over 50 per cent. of the cases complicating appendicitis there are 2 co-existing abscesses, 1 above and 1 below the liver. For this reason the writers advocate a **retroperitoneal operation**. The incision is made posteriorly on the 12th rib to within 4 centimeters of the midline, the entire 12th rib is resected subperiosteally, the muscles freed from the renal fascia, blunt retractors inserted to elevate and protect the diaphragm and pleura, the abscess approached by blunt dissection, and the subhepatic and suprahepatic spaces explored with straight and curved needles, respectively. Large rubber tubes and **iodoform gauze** are used for drainage. A co-existing empyema can be drained through the same incision. Healing time is shortened by the retroperitoneal operation; as soon as drainage has ceased and the drains are removed, the walls of the canal fall together and obliterate the cavity. Nather and Ochsner (Surg., Gyn. and Obst., Nov., 1923).

If the accumulation is anterior, it is best approached by a high right rectus incision; if posterior, by resection of the 10th rib in the posterior axillary line under local anesthesia. The pleura is carefully pushed forward, the costophrenic space entered, and the diaphragm seen. A large aspirating needle is pushed through the diaphragm, the pus located, and a small opening made in the diaphragm and enlarged by stretching with scissors so that a large rubber drainage tube may be inserted. The pleura, if accidentally opened, should be closed if it contains no fluid, and the wound packed with gauze for 24 to 48 hours to allow adhesions to wall off the pleural cavity.

J. Douglas (Annals of Surgery, June, 1924).

CHRONIC PERIHEPATITIS.—

This condition may be local or general. *Local* perihepatitis is always secondary. It is seen, for example: Around the gall-bladder in some cases of gall-stones; over a tumor in the liver; at the point of adhesion to the liver of an ulcerated stomach or intestine; as the result of a local tuberculous or carcinomatous deposit; and in many cases of venous obstruction whether from cardiac or pulmonary disease. It may result also from pressure, as in the furrows produced by tight lacing or constriction of the liver from any cause.

General perihepatitis is a very different condition. W. Hale White gives a valuable account of the condition based on the records of Guy's Hospital. In it "the whole capsule becomes thick, opaque, and white, . . . easily peels off the subjacent liver, the surface of which is smooth; and for some unexplained reason it is quite common to find the inferior edge folded up on to the anterior surface of the liver." This thickened capsule is often pitted deeply. The liver is usually slightly atrophied, but otherwise little altered. The thickened capsule does not seem to cause pressure upon the vessels at the transverse fissure. The capsule of the spleen and the general peritoneum are usually also thickened. The omentum may be thickened and contracted, forming a tumor across the abdomen.

Of the 22 cases analyzed by White in 19 there was chronic granular kidney, and he thinks the chronic peritonitis and general perihepatitis should be regarded as a sequel to the

renal disease. Ascites, resulting probably from the chronic peritonitis, is nearly always abundant and requires repeated tapping. These cases are doubtless frequently looked upon as cirrhosis of the liver. Further study of the condition is much needed.

Antipyrin salicylate, in 10-grain (0.65 Gm.) doses, given every two to four hours, relieves the symptoms of chronic universal perihepatitis, and limits the duration of the exacerbations to a very few days or sometimes hours. Usually at the expiration of thirty hours the patient regains his normal condition. Wilcox (Mthly. Cyclo. and Med. Bull., July, 1911).

JAUNDICE (ICTERUS).

DEFINITION.—This is not a disease, but only a symptom group, occurring under a variety of conditions and characterized by a yellowish discoloration of the skin, tissues, and fluids of the body with bile pigment, and the excretion of the pigment in the urine.

It has been customary to classify all cases of jaundice into the two great groups of obstructive and non-obstructive jaundice, but, the more thoroughly the pathology of the condition is investigated, the greater is the number of non-obstructive cases that are found in reality to be obstructive, and in time it is probable that in all conditions jaundice will prove to be obstructive in origin.

William Hunter originally designated the two groups of jaundice as *obstructive* and *toxemic*; these seem to be the most suitable terms at present available. The obstructive group includes all cases dependent on palpable obstruction; and the toxemic those occurring in connection with some general infection. Even what

is characterized as the toxic hemolytic or hematogenous form of jaundice is now recognized as fundamentally obstructive in character.

Jaundice resulting from mental emotion, usually of a depressing nature, cannot be placed in either group; its nature is quite uncertain. Numerous cases due to shock have, however, been reported.

Jaundice from suppression of liver function cannot now be accepted as possible, as bile pigment can only occur as the result of hepatic cell activity. Further, the removal of the liver or the complete severance of its connections by ligature does not cause jaundice.

As emphasized by Hamel, the blood-serum is found stained in icterus, even in the mildest grades and though the urine at the time show absolutely nothing. A simple procedure for making the diagnosis is to puncture the ear or finger and fill several capillary tubes, $1\frac{1}{2}$ mm. in diameter and 10 mm. long, with blood; the tubes are then closed at each end with sealing wax, placed vertically, and observed after a few hours, when the serum and blood have separated. A yellow tinge to the serum is an early indication of jaundice.

OBSTRUCTIVE JAUNDICE (HEPATOGENOUS JAUNDICE; EXTRAHEPATIC JAUNDICE).—

This type includes the cases due to mechanical obstruction in the hepatic duct or common bile-duct, irrespective of any changes of the blood or bile. As originally classified by Murchison, its causes are as follows:—

1. Obstruction by foreign bodies within the duct, as gall-stones, inspissated bile, parasites, etc.

2. Obstruction by inflammatory tumefaction of the duodenum, or of the lining membrane of the duct, with exudation into its interior.

3. Obstruction by stricture or obliteration of the duct, as may result from perihepatitis, or from a cicatrix in the duct or at its mouth in the duodenum.

4. Obstruction by tumors closing the orifice of the duct or growing into its interior.

5. Obstruction by pressure on the duct from without by (a) enlarged glands, (b) hepatic tumor, (c) tumor of the pylorus, (d) tumor of the pancreas, (e) tumor of the kidney, (f) omental tumor, (g) an abdominal aneurism, (h) fecal accumulation in the colon, or (i) ovarian or uterine tumors.

From 600 operative cases of jaundice, Riedel concluded that ineffectual gall-stone attacks in which the stone remains quiescent in the gall-bladder neck or in the cyst duct are unassociated in 90 per cent. of the cases with icterus. The majority of the patients, therefore, have no icterus during their first attacks of gall-stone colic. In 10 per cent. of the ineffectual attacks icterus ensues even when the calculus remains passively in the gall-bladder neck or in the cystic duct. This jaundice is of an inflammatory and mostly septic type. It originates through an extension of the inflammation to the bile passages of the liver or to the liver structure itself. In cases in which there are calculi situated high up in the hepatic duct, with displacement and kinking of the duct, a mechanical factor is added to the inflammation.

Experiments upon the relationship of the gall-bladder to the development of jaundice. Animals in which the common bile duct is obstructed and the gall-bladder left intact do not have an appreciable amount of bile pigment in the urine for 36 to 48 hours after the operation. Only a faint trace of bilirubin, if any, is found in the blood-plasma at the end of 48 hours. The scleræ do not develop an icteric tinge for 48 to 72 hours.

Usually 48 hours elapse between the duct obstruction and the first definite evidence that jaundice is developing.

The subsequent development of icterus and the accumulation of bilirubin in the blood are also slow. Mann and Bollman (Jour. of Lab. and Clin. Med., Apr., 1925).

Case of seeming catarrhal jaundice in a young woman, unaccompanied by fever or pain, and found due to obstruction of the common duct by ascarids. Transient improvement following the expulsion of several parasites led to the diagnosis, and definite recovery followed vigorous antiparasitic treatment. In cases of catarrhal jaundice of uncertain nature, the stools should be examined for ova. Labbé and Denoyelle (Bull. Soc. méd. des hôp. de Paris, May 1, 1925).

General Symptoms.—The color of the skin varies according to the intensity and duration of the jaundice. In cases of catarrhal jaundice with sudden obstruction the surface becomes rapidly stained a deep yellow. When jaundice has existed for a considerable time it changes to a greenish hue, which gradually passes into a dark-olive color, doubtless on account of the action of the air on the bile pigment in the skin. This very dark color, known as "black jaundice," though not pathognomonic of cancer in the liver, is rarely produced by any other disease. The icteric hue shows most distinctly on the pallid parts and to a much less degree on highly-colored parts, as the lips, florid cheeks, mucous membrane of the mouth, etc. We, therefore, look to the conjunctivæ for the first signs of icteric discoloration.

Many of the secretions are also colored with bile pigment. The sweat is yellow and stains the patient's linen. The tears and milk may also be colored, but the saliva is not stained nor do the secretions of the mucous membranes, not even of the bile-ducts and gall-bladder, contain any bile.

Inflammatory exudates, as the sputa of pneumonia, are bile stained, as are

also the exudates into the various serous cavities.

Since the removal of diffusible substances in the blood is chiefly by the kidneys, it follows that the urine contains more of the biliary coloring matter than any other secretion. It may be present in the urine even before it appears in the conjunctivæ. The color of the urine may vary from a barely perceptible greenish-yellow to a dark-brown or even black color. Bile pigment is invariably present in the urine in jaundice, except in chronic cases in which the obstruction to the bile flow is suddenly removed, when the icteric hue of the skin will persist after the blood has been cleared of the bile pigment. Bile-stained urine foams readily when shaken, and the froth is of a yellow color. Rhubarb and santolin, when administered, produce a similar color in the urine, but the froth is not yellow; the addition of caustic potash causes a red coloring of the fluid and the tests for bile pigments are not obtained.

Gmelin's test is usually employed to determine the presence of bile pigment, but it may fail to give a reaction even in the presence of 5 per cent. of bile. It is best made by placing a few drops of common nitric acid and of the urine on a white, flat surface and then causing them to run together. A play of colors results at the margin of contact, rapidly passing through various shades of green, blue, violet, and red, finally becoming a dirty yellow.

The following modification of it is much more delicate, revealing even 0.2 per cent. of bile, and should be employed in doubtful cases: "To 50 c.c. of urine add 5 c.c. of 10 per cent. barium chloride solution and 5 c.c. of chloroform. Shake for several minutes. Set

aside for ten minutes. The chloroform and precipitate of phosphates fall down, carrying with them all the bile pigment. Now draw off the chloroform and the precipitate with a pipette. Place in a flat dish, and set over a basin of hot water until all the chloroform has evaporated. Allow to cool and pour off any fluid from the precipitate. The latter will be yellowish. Place impure nitric acid in drops here and there on the surface of the precipitate. If bile pigment is present a play of colors appears round each drop." ("Clinical Methods," by Hutchinson and Rainy.)

The stained cellular elements in the urine afford a reliable test for the presence of bile pigment. In chronic cases the urine may contain albumin and pigmented tube casts. In those slight forms of jaundice in which bile pigments do not appear in the urine in appreciable quantity the spectroscope furnishes a very delicate and accurate test.

Hedenius's Test.—The following recommended as a simple method of detecting bile pigment in icteric fluids: To about $1\frac{1}{4}$ fluidrams of serous fluid add twice or thrice its volume of concentrated alcohol, and shake the mixture. Add as many drops of hydrochloric acid (10 to 25 per cent.) as will be required to dissolve the precipitate caused by the addition of the concentrated spirits, when the fluid will become clear. Bring the fluid to a boil, and if bile pigment be present a blue-green color will appear within a minute or so. In a serous exudation containing only 1 part of bilirubin to 250,000 parts of fluid, the blue-green color became very conspicuous. When it is desired to ascertain the presence of an insignificant quantity of the coloring matter of the bile in concentrated fluids

rich in albumin, the author proceeds as follows: To $\frac{3}{4}$ or 1 fluidram of the fluid add 4 or 5 times its volume of concentrated spirit, which will cause the precipitation of all the protein substances present. Shake well several times and filter the fluid. Add several drops of hydrochloric acid and boil, when, if bile pigment be present, a delicate blue-green color will appear.

Jaundice may be distinguished from the yellow hue caused by malaria, cancer, lead poisoning, and some kidney affections, according to Inglis, by placing a few drops of the urine in a porcelain dish and causing a couple of drops of nitric acid to flow against it. If bile pigment be present, a greenish tint will result, followed by blue, violet, and a yellow or brown.

New test for bile pigments in the urine, bile and blood serum, based on the observation, made in testing urine for indican, that all urines containing bile pigments when treated with Obermayer's reagent become a deep greenish blue at once. In applying the new test to the *urine*, 0.5 c.c. of Obermayer's reagent is added to 5 c.c. of urine. If bile pigment is present, a deep green at once appears. If there is only a faint trace, the color will appear after standing a few minutes in warm water. *Bile* diluted 1:1000 gives an immediate reaction. In the case of the *blood serum*, 4 c.c. of 95 per cent. alcohol are added to 2 c.c. of serum to precipitate the proteins, and the mixture is centrifugated. The clear supernatant fluid is withdrawn, and 0.5 c.c. of Obermayer's reagent added. The green color appears in a few seconds. The test is more sensitive than the Gmelin and Rosenbach reactions, giving a response up to dilutions of 0.000033 Gm. of pure bilirubin per c.c. R. Kapsinow (Jour. Amer. Med. Assoc., Mar. 1, 1924).

Ehrlich's Aldehyde Test.—This is a test for urobilinogen, which arises from

the transformation of bile in the intestine, largely by the action of bacteria, and which can appear in the urine only with disturbed action of the liver-cells. It is performed as follows; A stock solution is made with paradimethylaminobenzaldehyde, 4 Gm.; hydrochloric acid, 40 Gm.; water and a few drops of alcohol, to make 200 c.c. One or 2 drops of this solution are added to 5 c.c. of fresh urine. In the presence of urobilinogen there develops, usually in the first few minutes, a rose-red color. Exceptionally, the extreme depth of color is not reached until $\frac{1}{2}$ to 2 hours have elapsed. The reaction is somewhat more common in dark than in light colored urines. In a dark, bile-laden urine bile pigments obscure the test. The urine with the reagent is then shaken with a few drops of chloroform, when the red color appears in the chloroform at the bottom of the tube.

Van den Bergh Test.—This is a test for the differentiation of obstructive from other forms of jaundice. The bilirubin content of the blood is taken as determining whether any given case of jaundice is to be classed as mechanical or due to insufficiency of hepatic function.

Bilirubin is normally present in the blood in a concentration of about 0.3 to 0.5 part in 200,000. Visible jaundice and excretion of bilirubin through the kidneys do not begin until a concentration of 4 parts in 200,000 is reached. Between these 2 concentrations there exists a state of mild hyperbilirubinemia or "latent jaundice" which has proven of some diagnostic significance. Detection of these slight excesses of bilirubin may be carried out by means of the Van den Bergh test or the Fouchet test.

The Van den Bergh test may be

either direct or indirect. In the *direct method*, 0.25 c.c. of Ehrlich's diazo reagent is added to 1 c.c. of the serum (obtained by centrifugation) in a small test-tube. In obstructive jaundice, the color changes from pale yellow to violet or pink, owing to the formation of azo-bilirubin. In the *indirect method*, which is positive in both obstructive and non-obstructive jaundice, 1 c.c. of serum is added to 2 c.c. of alcohol and centrifugated; 1 c.c. of the supernatant fluid is then withdrawn and 0.25 c.c. of diazo reagent added to it. The color change in a positive test is the same as in the direct method. In normal blood the change is always faint or absent.

The writer found the Van den Bergh test regularly negative in 19 normal subjects and positive in 11 cases with obstruction of bile ducts from cancer or gall-stones. In 3 cases of jaundice with enlarged liver in secondary syphilis and 1 of jaundice in lobar pneumonia, however, the test was likewise positive, contrary to expectations, such a result pointing to an obstructive type of jaundice. Sabatini (Policlin., Oct. 1, 1922).

The Van den Bergh test permits of distinguishing a frankly hemolytic from a frankly obstructive jaundice, but is of little value in differentiating icterus due to liver cell damage from other types of jaundice. It is helpful in distinguishing pernicious from secondary anemia, and when applied to other fluids, in deciding whether a hemorrhagic effusion or cerebrospinal fluid was previously blood-stained or had been stained by blood at the time of puncture, and whether aspirated blood has come from a hematoma or not. In conditions giving only the indirect reaction, bilirubinuria never occurs. C. H. Andrewes (Quart. Jour. of Med., Oct., 1924).

The bilirubin in obstructive jaundice is identical with that in hemolytic jaundice. The direct diazo (Van den Bergh) reaction is dependent upon the

existence of free bilirubin in the blood serum; the indirect reaction, upon combination of bilirubin with the proteins of the blood plasma. The intensity of the phenomena of adsorption is related to the amount of proteins and cholesterin in the blood. Piotrowski (*Arch. des mal. de l'app. digest.*, Oct., 1925).

Fouchet Test.—This is performed with Fouchet's reagent, which is made up of trichloroacetic acid, 5 c.c.; 10 per cent. ferric chloride solution, 2 c.c., and distilled water, 20 c.c. In carrying out the test, 3 to 5 drops of this solution are added to an equal amount of the blood serum and mixed on a white porcelain surface. A green color, specific for bile pigment, develops if bilirubin is present to the extent of 1:60,000 or over. There is, therefore, no reaction whatever with normal serum.

From comparative tests, the writers were led to recommend the Fouchet test in preference to the Van den Bergh test for clinical purposes, it being simpler and less sensitive and reacting only in the presence of a pathologic amount of bilirubin. In 29 cases of undoubted cholecystitis without evident jaundice, hyperbilirubinemia was shown by these tests to exist in 93 per cent. of cases during the attack and in 73 per cent. during the interval. It is of value in deciding between cholecystitis and gastric or duodenal ulcer or carcinoma. J. C. Friedman and D. C. Straus (*Jour. Amer. Med. Assoc.*, Apr. 19, 1924).

Since, in jaundice, no bile enters the intestine, the feces are pale or clay-colored, on account of the large amount of fat present. They are pasty and usually fetid. Strümpell held that the clay color of the stools is due to the undigested fat, and in jaundiced patients who are fed on fat-free food this peculiar odor is not present. There is usually constipation, but diarrhea is not infrequent, owing to the decom-

position in the intestines. There may be no derangement of the stomach, but often there is loss of appetite, coated tongue, foul taste, fetid breath, and epigastric fullness after food.

Slow pulse is very characteristic; it is usually from 40 to 60, but may be down to even 20 per minute. Such pulse changes are more frequent in catarrhal jaundice and are not usually of unfavorable significance. The respirations are usually normal, but may fall to 10 or less per minute.

In many protracted cases there is a marked tendency to hemorrhages, especially to purpura and to subcutaneous extravasations. The blood requires in some cases eleven or twelve minutes to coagulate instead of three or four, as in normal states.

Surgical operations should be undertaken in case of chronic obstructive jaundice only with due regard to this change in the blood. Certain preparatory prophylactic measures are in order in such cases (see under Treatment).

Pruritus is often a distressing symptom in the chronic forms of obstructive jaundice. It occasionally precedes the onset of the jaundice. It is worse at night and may be general or localized. Scratching gives rise to various eruptions. Sweating is frequent. Urticaria, lichen, and boils may be present, as may also xanthelasma.

Cerebral symptoms may be marked, including irritability, great despondency, and even melancholia. There are often headache, vertigo, and dullness; there may be sleeplessness. The vision may be affected in various ways; there may be nyctalopia, or improved vision in obscurity; objects may appear yellow, or there may be hemeralopia, or very difficult vision.

Specially severe symptoms may develop in persistent jaundice and quickly prove fatal. Usually there is slight fever, rapid pulse, emaciation, and mild delirium. From this typhoid state the patient may soon become comatose or develop convulsions. This condition was formerly denominated *cholemia*, or sometimes *cholsteremia*. Its cause is uncertain, but probably most cases are due to a "terminal infection."

In many patients jaundiced from gall-stone disease the clotting time is normal, and there is no inclination to hemorrhage. In very grave cases of jaundice in which there is a tendency to hemorrhage the ability of the blood to clot is very much lowered. This is independent of the intensity of the jaundice. When in patients with jaundice, who come for operation, an examination shows a retarded clotting time of the blood, we may assume the existence of an advanced stage of a liver affection, which renders the case no longer suitable for operation. Kunika (Deut. Zeit. f. Chir., cxviii, S. 574, 1912).

Etiology.—The duration of obstructive jaundice depends upon the nature of the cause. A simple catarrhal jaundice may last but a few days, while chronic cases may continue many months, though frequently characterized by periods of improvement.

The following significant points must be noted in the diagnosis of chronic catarrhal icterus: 1. Icterus, preceded by hepatic congestion, and by copious biliary diarrhea. 2. Colorless feces of long duration, but with occasional recurrence of the normal color. 3. Diminished secretion of urine, the quantity becoming normal during the periods of improvement. 4. Diminished urea, with normal amount during the periods of amelioration. 5. Diminished quantity of biliary pigment, but toward the end of the disease the urine becomes red in color rather than green. 6. Con-

stant glycosuria after the fifteenth day of the disease. 7. Intermittent elimination of methyl blue. 8. Purpuric spots after the second month, temperature between 38° and 40° C. (100.4° and 104° F.), and a general adynamic, typhoid condition. Audibert (Revue de méd., June 10, 1907).

Case of chronic jaundice caused by tuberculous peritonitis which persisted 15 months. The symptoms caused the authors to hesitate between cancer and lithiasis. An operation showed neither, but demonstrated the presence of extensive peritoneal adhesions with contraction almost to the point of obliteration of the bile ducts. Careful study of the case convinced them that this was due to an old tuberculous peritonitis, in which the inflammatory process had involved the bile ducts. Mouisset and Gaté (Lyon méd., Mar. 2, 1913).

Jaundice as a symptom is difficult to trace to its cause. In approximately 50 per cent. of the cases seen, the absorption of bile was due to obstruction of the common duct by gall-stones; in 20 per cent. of all cases it was due to absorption of bile in the liver, or infective or catarrhal jaundice without duct obstruction. From 5 to 8 per cent. were due to serious infection of the gall-bladder, possibly gangrene with or without stones. These were usually accompanied by a degree of pancreatitis with marked swelling of the lymph glands on the 3 ducts, all persons having 1 on each duct, but no one more than 2. Jaundice from cancer represented but 15 per cent. of the cases; one-half of them were from cancer of the liver, the other half from cancer of the pancreas or of the gall-bladder and ducts. C. H. Mayo (N. Y. Med. Jour., Mar. 13, 1920).

Treatment.—The cause of the jaundice must be determined at the earliest possible moment and the treatment be based on the conclusion arrived at. As emphasized by Cammidge, a diagnosis

of gall-stones obstructing the bile-duct, made on the clinical data and confirmed by an examination of the excreta, calls for immediate **operation**, as the only likely spontaneous cure is nature's crude and dangerous remedy of making a fistula by which the stone may escape into the duodenum, or elsewhere.

Catarrhal jaundice frequently clears up spontaneously, but if after six weeks of **rest in bed**, with **dieting** and **medical treatment**, the jaundice persists and the urinary "pancreatic" reaction is positive, it is advisable to invoke the aid of the surgeon to perform a **short-circuiting operation** to avoid further damage to the pancreas. In the last stages of malignant disease **operation** is only likely to shorten the brief span of life still left to the patient, but in the earlier stages much may be done to make existence more bearable by a **cholecystotomy** or **cholecystenterostomy** to relieve the intolerable itching of which complaint is chiefly made. At the same time it is well to bear in mind that in many cases diagnosed clinically as inoperable carcinoma of the pancreas, it has been shown on chemical examination of the urine and feces, and by the after-history, that the patients were suffering from chronic inflammation of the gland capable of retrogression.

The following causes of chronic jaundice must be taken into consideration: (1) Common duct cholelithiasis; (2) chronic pancreatitis; (3) simple stricture of the common bile-duct; (4) inflammatory adhesions causing pressure on, or stenosis of, the hepatic or of the common bile-duct; (5) hydatid disease of the liver pressing on, or discharging into, the bile-ducts; (6) gummata implicating the duct; (7) chronic catarrh of the bile-ducts; (8) cancer of the common bile-duct; (9) cancer of the head

of the pancreas; (10) cancer of the liver associated with jaundice due either to catarrh or to pressure; (11) cirrhosis of the liver; (12) other rare causes, such as aneurism of the hepatic artery or of the aorta, and other tumors of the liver, gall-bladder, pylorus, or kidney, pressing on or occluding the common bile-duct.

Surgery holds out a good prospect of cure in the first five causes enumerated; **medical treatment** alone is advisable for causes 6 and 7, and in the remainder with certain exceptions relief can be hoped for only from medical or **surgical treatment**. As in many other conditions, pain is the most valuable guide in establishing a differential diagnosis between those possible causes. A painless onset of chronic jaundice points to chronic catarrh, due either to cancer of the liver or of the head of the pancreas, or both. On the other hand, pain in the upper abdomen, followed within twenty-four or thirty-six hours by jaundice, strongly suggests cholelithiasis. Here the jaundice is less intense and is pretty certain to be accompanied sooner or later by intermittent fever, chills, and sweats, with very marked icteric fluctuations. Ascites is very suggestive of malignant disease; it points to it perhaps more strongly than any other single symptom. Other diagnostic anteoperative aids are as follows: Jaundice in cancer of the bile-ducts and head of the pancreas tends to become absolute; in almost every other condition it is variable. Fat in the feces and glycosuria, with very rapid wasting, are very suggestive of pancreatic trouble. If the anteoperative signs be difficult of true interpretation, those found after the abdomen is opened call for as much or more acumen. Adhesions in the neighborhood of a contracted gall-bladder suggest stones, but this may be induced by a simple pyloric ulcer. If the head of the pancreas be swollen and harder than normal, one should not too hastily pronounce it cancer; it may very probably be a simple chronic pancreatitis, curable

by cholecystotomy. Again, the discovery of enlarged glands does not warrant a gloomy prognosis, for discrete nodules are frequent in common duct cholelithiasis and in chronic pancreatitis. If they are fused, however, the outlook is bad.

The treatment depends on the diagnosis. 1. If it be doubtful, an **exploratory incision** is indicated if the patient's general condition will permit. 2. If malignant disease be positively diagnosed, operation can, with some few exceptions, do but little good save when all the diseased tissue can be removed. 3. If gall-stones or any of the first five factors be diagnosed, **operation** is decidedly advisable if the patient be at all able to bear it. A. W. Mayo Robson (Brit. Med. Jour., Jan. 18, 1902).

All patients suffering from chronic obstructive jaundice should be **operated** upon, this affording the only hope of relief. Internal drainage of the bile ducts is preferable to external drainage; it is also desirable, when possible, to anastomose around inoperable growths in the intestine to avoid the formation of an artificial anus. The slightly greater risk involved in anastomosing the gall-bladder over simple drainage is more than offset by the increased comfort of the patient plus the added advantage of retaining the biliary secretion. Besides, in the event of a cure by external drainage, a secondary operation is necessary to close the fistula. The writer found it easier to unite the gall-bladder to the stomach than to the duodenum, and since the passage of bile through the stomach is harmless, he considers **cholecystogastrostomy** the operation of choice. Downes (Med. Jour. and Rec., Jan. 2, 1924).

At the Mayo Clinic, to reduce the deaths from oozing hemorrhage in jaundiced cases, there is begun, about 4 days before operation, a daily course of **intravenous injections** of 5 to 10 c.c. ($1\frac{1}{4}$ to $2\frac{1}{2}$ drams) of 10 per cent. **calcium chloride** solution. **Calcium**

lactate is also given by mouth. The patient takes large quantities of **carbohydrates** to protect the body proteins from bile toxemia, and a **Murphy drip** of 15 per cent. **glucose** solution in tap water is given 1 hour on and 1 hour off. **Water** is taken in large amounts.

Preoperative preparation in 34 cases of obstructive jaundice prevented death from hemorrhage in all, only 2 bleeding from their wounds. The coagulation time was estimated by Lee and White's method before administering **calcium chloride** intravenously each day and on the morning of the day of operation. If the coagulation time of the venous blood had not been lowered to less than 9 minutes, operation was postponed until such reduction was obtained. Even where it was 9 minutes or less, in some cases calcium chloride was given intravenously as a precaution against postoperative hemorrhage, 3 injections of 5 c.c. (80 minims) of a 10 per cent. solution being administered in these patients. W. Walters (Minn. Med., Jan., 1923).

The treatment of catarrhal jaundice *per se* requires measures addressed to the catarrhal state. This is accomplished by inducing watery stools by means of saline aperients such as **magnesium citrate**, **Rochelle salts**, **Epsom salts**, and **waters**, especially **Saratoga** or **Apenta**. Free purgation is not necessary, but aperient doses should be taken daily. Mineral waters, those of **Vichy** or **Vals**, for instance, should be used freely to increase the proportion of fluid passing through the intestine and liver. When mild purgation is necessary, **calomel** is to be preferred. Hepatic antisepsis is thought to be aided by the use of **sodium salicylate** in 10-grain (0.6 Gm.) doses, or **methenamine** in 5-grain (0.3 Gm.) doses four times daily. If the jaundice be due to calculus, the

measures recommended under CHOLELITHIASIS are indicated.

Good results in simple catarrhal jaundice by rectal administration of a solution of **sugar**, 45 Gm. (1½ ounces); **methenamine**, 1.5 Gm. (23 grains), in 1 liter of tepid water, by the drop method. The amount introduced begins with ½ liter, later increased to 2 or 3 liters in as many days. Weil (Bull. méd., June 12, 1920).

Insulin injected in various liver disorders. Favorable effects on jaundice and on the subjective disturbances were noted. In these cases the insulin causes retention of water in the blood. The blood sugar, generally low, declines further under the insulin to a level lower than in other individuals. Klein (Zeit. f. klin. Med., Nov. 16, 1925).

Non-surgical gall-bladder drainage has proven of value in these cases.

In several cases of acute catarrhal jaundice, the author gave 1½ grains (0.1 Gm.) of **calomel**, injected into the **duodenum** 50 c.c. of 25 per cent. **magnesium sulphate** solution, and aspirated the duodenal contents over a period of 2 hours. At the first sitting 50 c.c. of fluid were recovered, but on the next day, upon repetition of the procedure, 250 c.c. were obtained, the calomel apparently inducing a copious flow of bile, which the magnesium sulphate brought promptly down into the duodenum by relaxing the outlet of the common duct. Rapid improvement and subjective relief followed this procedure. A. H. Hopkins (Med. Clin. of No. Amer., Mar., 1920).

[See also GALL-BLADDER, NON-SURGICAL DRAINAGE, p. 424, this Volume.]

Another feature of importance is the use of foods which do not require bile to facilitate digestion and absorption and prevent decomposition, and which are not likely to irritate the intestinal mucosa. **Fats, oils, and irritating condiments should be avoided, and skimmed milk, animal broths, egg albumin, and the free use of water**

are indicated. **Warm bathing** assists elimination, and relieves the pruritus.

Cold injections of water or normal saline solution have been recommended by Polain-Cartier on the ground that they favor biliary flow by promoting peristalsis.

It is unnecessary to resort to an exclusive milk diet. Along with 1 liter (quart) of milk or skimmed milk per diem various vegetable articles of food, e.g., purées of dried vegetables or potatoes, pastes, such as macaroni, well-cooked green vegetables, or cooked fruits, may generally be permitted.

The writer prefers not to give calomel, but advises the following:—

R *Sodium salicylate*,

Sodium benzoate .of each gr. v (0.3 Gm.)

Powdered rhubarb gr. iiss (0.15 Gm.).

M. et ft. pulvis.

Three cachets, each containing these ingredients, should be taken daily, before meals. Cachets or pills of **oxgall** may be employed instead. **Methenamine** should be administered without fail in 4 cachets of 0.5 Gm. (7½ grains) each per diem.

Metecorism may be counteracted by giving, after each of the two heavier meals of the day, a cachet containing:

R *Charcoal*,

Bismuth sub-salicylateãã gr. vj (0.4 Gm.).

Powdered nuxvomica gr. ⅓ (0.02 Gm.).

M. et ft. pulvis.

Itching of the skin, often severe, requires the taking of a daily **alkaline bath** of ten minutes' duration, in water containing from 100 to 150 Gm. (3½ to 5 ounces) of **sodium bicarbonate**, at a temperature of 35° C. (95° F.). The bath should be followed by application of a **hot lotion of coal tar** (2 tablespoonfuls to the liter), of **vinegar** to which **phenol** has been added, or of 2 per cent. **chloral hydrate**. After the lotion, the follow-

ing inert powder should be dusted over the skin, without previous drying:—

℞ *Bismuth subcarbonate*,
Zinc oxide,
 of each 3v (20 Gm.).
Powdered starch. ʒii¼ (68 Gm.).

M. et ft. pulvis.

If the itching continues notwithstanding, a mixture of 1 part of **chloroform** with 3 parts of **glycerin** may be painted over the skin two or three times daily. Finally, baths of **static electricity** with effluve may be administered; these often relieve itching of hepatic origin more promptly than any other measure. Oppenheim (N. Y. Med. Jour., from Progrès méd., Jan. 13, 1912).

The treatment of catarrhal jaundice consists first in hygiene and diet, the patient being put to bed and on a milk diet. Intestinal poisoning is thus combated. About 3 quarts of skim milk daily are prescribed, but **kefir** or **yoghurt** may be substituted. Ordinary diet should be resumed very gradually, eggs being cautiously added and only the white meats used at first. Grapes are thought to be a powerful hepatic stimulant, and lemon juice has its partisans. Plenty of water is given to help diuresis; this is important, and mild mineral waters may be used. Cold enemata, twice a day, are advised. **Benzonaphthol** and **salacetol** are given to combat the intestinal sepsis; a **calomel** purge follows at the end of the first week, then **opotherapy** by means of half a dozen daily capsules of bile. Pills of **extract of liver** are sometimes substituted. At the end of the third or fourth week, **hexamethylenamine** and **sodium salicylate** are indicated. If the liver remains enlarged the patient is ordered to one of the mineral spring resorts, or a powder may be given of **sodium bicarbonate**, 8 Gm. (2 drams); **sodium phosphate**, 4 Gm. (1 dram); **dried sodium sulphate**, 2 Gm. (½ dram), dissolved in a quart of hot

water and taken three times daily one hour before meals. Jaundice is often a sign of infection. If it persists, repeated **calomel** purges are given, the bile opotherapy is continued; also the cold enemata.

Itchiness of the skin is best combated by very hot lotions containing alcohol or vinegar or dilute carbolic acid, or by zinc oxide ointment containing a small proportion of menthol. Hemorrhage is met with calcium chloride and opotherapy. Lereboullet (Paris méd., Sept. 14, 1912).

For the treatment of itching of jaundice the following lotion is recommended:—

℞ *Resorcinolis*,
Mentholis .. āā gr. xv (1 Gm.).
Hydrargyri chloridi corrosivi gr. iij (0.2 Gm.).
Glycerini f3v (20 c.c.).
Aqua cologniensis f3iij (100 c.c.).
Alcoholis f3xiiij (400 c.c.).

M. et ft. solutio.

Sig.: To be used as a wash.

L. Aldor (Nouveaux remèdes, Jan. 24, 1913).

TOXEMIC JAUNDICE (HEMOLYTIC JAUNDICE; HEMATOGENOUS JAUNDICE; HEMOHEPATOGENOUS JAUNDICE; JAUNDICE OF POLYCHROMIA; NON-OBSTRUCTIVE JAUNDICE).—In this form there is said to be no obstruction in the bile passages. This in most, if not all, cases is not correct, because, although the larger ducts are free, the bile radicles within and around the hepatic lobules are obstructed to a greater or less extent by swelled epithelium, pigment granules, and crystals of leucin and tyrosin. The obstruction in these cases is shifted from the larger ducts to the bile radicles, many of which escape, so that the obstruction is rarely complete. The cause acts on

the liver substance in general and must, therefore, be toxic and conveyed to it by the blood, either of the general or the portal circulation. The toxin acts on the blood, and in its excretion by the liver leads to the secretion of a viscid bile, to irritation of the bile radicles, and it may be to degenerative changes in the liver cells.

Hunter recognized three groups of this class of cases:—

1. Jaundice due to poisons, as toluylendiamin, phosphorus, arseniuretted hydrogen, picric acid, and snake-venom. This type includes post-operative jaundice, due to the toxic action of the anesthetic, chloroform especially, and those following injections of salvarsan.

Case of a man aged 32 years in whom a first injection of 0.5 Gm. ($7\frac{1}{2}$ grains) of salvarsan was followed by severe headache, backache, vomiting, diarrhea, and motor weakness, all of which had disappeared by the next day. A second injection of 0.6 Gm. (10 grains), given six days after the first, at first seemed well borne; but on the following day there appeared similar symptoms, together with fever and pains throughout the body. Twenty-four hours later signs of oncoming jaundice were observed, and eight days after the second injection marked icteric hue had appeared. Treatment proved utterly unavailing, the jaundice persisting eight months. The stools were white, the urine discolored. The body weight fell rapidly from 80 to 58 kg. (176 to 127 pounds) and the hemoglobin to 60 per cent. E. Giradet (*Revue méd. de la Suisse Romande*, Dec., 1913).

Many cases of jaundice among munition workers, due to trinitrotoluol, were reported during the European war. Tetrachlorethane has also at times caused jaundice. The skin is believed the main channel of absorption of these poisons. Ac-

cording to M. J. Stewart (*Brit. Med. Jour.*, Feb. 3, 1917) the associated liver lesion lies somewhere between subacute yellow atrophy and ordinary multilobular cirrhosis of irregular distribution. Dermatitis, gastritis, and blood changes typically accompany the toxic jaundice. W. J. O'Donovan (*ibid.*) states that the jaundice may supervene from the fourth day to the ninth month of munition work, and may first appear after a period of freedom from exposure extending as long as 2 months. The prognosis is uncertain, coma or convulsions suddenly setting in sometimes when recovery was expected. According to W. R. Smith (*ibid.*) constipation is an almost invariable symptom. **Absolute rest in bed** is essential even in the mildest cases, and where there is a tendency to hemorrhage **calcium chloride** may be used. EDITORS.

2. Jaundice occurring in various specific fevers, as yellow fever, malaria, pyemia, typhoid, typhus, and scarlatina.

In a man of 46 who died after three weeks of an infectious jaundice a paratyphoid bacillus was cultivated from the blood during life and from the liver, spleen, etc., *post mortem*. It is probable that many cases of so-called catarrhal icterus are in reality a general infection with secondary localization in the biliary apparatus. O. Scheel (*Norsk Mag. f. Lægevidenskaben*, Jan., 1910).

The writer was able to cultivate the pneumococcus from the blood in 3 cases of pneumonia complicated with jaundice. Autopsy revealed inflammation in the parenchyma of the liver; the inflammation in the vessels and ducts was secondary. Lemierre (*Presse méd.*, Feb. 2, 1910).

3. Jaundice occurring in obscure infective conditions, as in epidemic, infectious, febrile, or malignant jaundice, icterus gravis, Weil's disease, and acute yellow atrophy of the liver. To this group probably belongs, in the light of modern work, the jaundice due to syphilis.

Case of fatal icterus due to secondary syphilis. Icterus appeared insidiously without apparent cause. The patient, a young woman, presented the stigmata of secondary syphilis, absence of pre-existent digestive troubles and of fever, and later a subnormal temperature, absence of bradycardia, nocturnal malaise which disappeared during the day, and finally the sudden development of the seemingly benign icterus into a malignant form. Sézary (*Presse méd.*, Sept. 26, 1908).

Case of icterus syphiliticus. The exanthem retrogressed under mercury salicylate. After the sixth injection the patient began to suffer from slight catarrhal symptoms of the intestine with some swelling of the liver. The course was favorable; there was absence of general, particularly cerebral, symptoms, and the absence of diminution in the size of the liver marked the affection clinically as a simple, perhaps somewhat intense, icterus syphiliticus præcox. After about two weeks leucin and tyrosin were found in the urine, which are usually met with in syphilis only in yellow atrophy of the liver. This raised the question whether, instead of a benign icterus, the case was not one of parenchymatous inflammation of the liver that would result in yellow atrophy. Busche (*Berl. klin. Woch.*, Feb. 7, 1910).

Syphilitic jaundice may appear even in the primary stage, but occurs oftener in the secondary stage. A skin eruption may co-exist. The condition is usually dependent on injury to the hepatic cells themselves. This injury varies in degree resulting in urobilinuria without jaundice or acute yellow atrophy. Since histologic and experimental studies have not as yet demonstrated the presence of spirochetes in the liver in such cases, the damage to the liver cells may be ascribed to the toxins of these organisms. Congenital weakness, intestinal and metabolic disturbances, as well as other infections, may operate as predisposing causes. Arsphenamin is likewise an important factor; poor or deteriorated prepara-

tions of the drug may be responsible, and there may also be a provocation of syphilitic liver disease by the drug. Less common, it seems, is a direct arsenical poisoning of the liver by the drug. Demonstration of leucin and tyrosin in the urine is useless in the differentiation of actual atrophy of the liver, for these products may be absent in atrophy and present in slight, transient jaundice. In the treatment of syphilitic jaundice the writer recommends mercury in the form of *novasurol* or, especially, *calomel* in small doses. Under such treatment even syphilitic atrophy of the liver is remediable in time. A. Buschke (*Zeit. f. ärztl. Fortb.*, xxi, 414, 1924).

In this class the jaundice is usually less intense than in obstructive jaundice. There is only a partial absorption of the bile pigment by the lymphatics of the liver. Bile appears in the stools at some period of the history; it may be in excess, causing very dark fecal discharges. It is thus distinguished from true obstructive jaundice in that the stools are not clay colored.

There is usually more constitutional disturbance than in obstructive jaundice. In severe cases this is very pronounced—high fever, dry tongue, delirium, subsultus, convulsions, hemorrhages from various parts, black vomit, all indicating severe constitutional infection.

Clinical Tests.—The Van den Bergh and Fouchet tests, recommended by various observers for the differentiation of obstructive from toxic jaundice, have already been described under Obstructive Jaundice. Other procedures—"tests of hepatic function"—have likewise been regarded as having some bearing on the etiology of jaundice. Of these, the alimentary levulosuria, phenoltetrachlorphthalein and hemoclastic tests have been described under CIRRHOSIS OF THE LIVER, Vol. III (*q.v.*).

The **indigocarmin test** may be performed, as described by Hatiéganu (*Ann. de méd.*,

Nov., 1921), by injecting intramuscularly 0.24 Gm. of indigocarmine in a warm solution in 20 c.c. of saline solution. Bile is then aspirated with the duodenal tube and shows the color of the stain in 20 minutes, with the maximum effect in 2 or 3 hours. In hepatic disease with jaundice, the stain fails to reach the duodenum, and its elimination is also delayed in pernicious anemia and in venous cirrhosis.

The **sodium salicylate test** is a simple procedure described by Roch (Rev. méd. de la Suisse rom., Apr., 1922), in which 0.04 Gm. ($\frac{2}{3}$ grain) of the drug is taken by mouth 1 hour after breakfast. Normally none can be detected in the urine in the succeeding 5 hours, as the liver does not allow this amount to pass, but in hepatic insufficiency the urine, dropped into 1 per cent. ferric chloride solution, produces a violet cloud.

With the Rosenthal phenoltetrachlorophthalein test, marked retention of the dye occurs in catarrhal jaundice; this persists for a considerable time following the disappearance of the icterus, strongly suggesting some distinct disturbance of the liver cells. In cirrhosis, retention of the dye may occur to a greater or less degree. In cancer of the liver it is always rather marked. In syphilis of the liver, retention may or may not occur, depending largely on the degree of involvement. In chronic cholecystitis, cholelithiasis and infections in which the liver itself is not severely involved, retention of the dye is never observed. Friedenwald and Morgan (Ann. of Clin. Med., Nov., 1925).

Bile pigment is considered to be formed of broken-down hemoglobin—hemoglobin without iron. The product is manufactured by the reticulo-endothelial system, represented by cells of the spleen and bone-marrow. With the liver entirely removed, the bile pigment is formed but not excreted; thus, the liver is mainly an excretory organ. The Van den Bergh test gives an estimate of the bilirubin curve and serves as an indication for or against operation. The dye retention test does not coincide with the amount of jaundice, for with slight jaundice there may be

considerable dye retention. In cirrhosis there is often much dye retention. In cholecystography, the time it takes for the opaque substance (taken with the evening meal) to reach the gall-bladder is estimated. In severe cases of liver obstruction the opaque substance does not reach the gall-bladder; in such cases, intravenous glucose injection may prolong life. C. S. McVicar (Jour. Amer. Med. Assoc., May 22, 1926).

All cases usually show: (1) Destructive changes in the blood; (2) alterations in the quantity and quality of the bile; (3) changes in the liver cells and bile-ducts, varying in degree according to the irritant power of the toxin.

Hemolytic jaundice was first described by Hayem in 1898 and occurs in a *congenital* or *familial* and, less commonly, in an acquired form. In the former the condition persists through life, but may not seriously impair the general health, aside from the attacks of fever, vomiting of bile and pain. In the *acquired* form, which may be either cryptogenetic or secondary to a number of diseases, chiefly infectious, the clinical course is more severe, frequently terminating in death; the anemia is more marked, but the jaundice itself often less marked or even lacking.

In the congenital type, the resistance of the red blood cells to hypotonic salt solution is reduced, as shown by Chauffard; laking may begin in 0.7 to 0.6 per cent. salt solution and be complete at 0.4 or even 0.45, whereas normally it begins only at 0.44 to 0.48 and is complete at 0.3. In acquired hemolytic jaundice, the resistance of the red cells is less constantly diminished and to a less degree. Splenic enlargement, sometimes to a large size, is almost constant in both types.

Both forms show a bright yellow

jaundice, differing from the general dull tint of icterus due to cirrhosis. The jaundice also varies in intensity from time to time, emotions and fatigue accentuating it, while it subsides during rest and in mountain air. The stools are not clay colored, and bilirubin is found only in small proportions in the urine.

Aside from the diminution of red cell resistance, there is also, according to Chauffard, a reduction of the average diameter of the red corpuscles and an anisocytosis. In one patient observed by Chauffard, the average diameter was from 3 to 5 microns. In obstructive jaundice, on the contrary, there is increased resistance and diameter. The disorder is also peculiar in the presence of many granular red corpuscles—manifestations of an abnormal, atypical, blood regeneration. There is absence of auto-agglutination and of auto-hemolysis.

The writer records 4 personal cases showing icterus, anemia, diminished corpuscular resistance and splenomegaly, with or without enlargement of the liver. The icterus was of the acholuric type and the blood serum contained bilirubin but no urobilin. The feces were acholic and only assumed their normal color during the hemolytic paroxysms. The blood showed secondary anemia, but not always the granular red cells mentioned by Chauffard. Lüdke (Munch. med. Woch., Oct. 1, 1918).

Familial nature of hemolytic jaundice illustrated by the Röschmann family, the record of which was brought down to date by the writer. The father and 6 members of his family had the disease, and **splenectomy** arrested it completely in all. The recent re-examination of the family showed that 11 of the 26 members of 3 generations had presented the family taint. Splenectomy in the mother did not prevent development of the hemo-

lytic jaundice in a child born 9 years later. In another instance the child has been free from the condition to date although the splenectomy was done during the pregnancy. Hemolytic jaundice can be transmitted by either sex to either sex. The results of splenectomy clearly point to the spleen as the organ responsible for the hemolytic tendency. Hattesen (Mitteil. a. d. Grenzgeb. d. Med. u. Chir., xxxvii, 293, 1924).

Case in a young woman illustrating the problems of differentiation between familial hemolytic jaundice and Banti's disease. There existed both jaundice and splenomegaly, and there was a family incidence. The blood picture was uninformative, the etiology unknown and the course symptomless. The decreased resistance to hypotonic salt solution pointed, however, to hemolytic jaundice as the correct diagnosis, since in Banti's disease, if there is any change in resistance, it tends toward an increase. Cocke (Amer. Jour. Med. Sci., Feb., 1925).

A small diameter but relatively normal volume of the erythrocytes observed in hemolytic jaundice. The apparent microcytosis disappears after splenectomy, but the fragility of the cells continues high. The change of shape of the cells is merely a secondary evidence of blood degeneration. Boros (Wien. Arch. f. inn. Med., Feb. 10, 1926).

The destructive blood changes in toxic jaundice may be shown by the occurrence of hemorrhages from the mucous surfaces, as of the nose and stomach. The black vomit of yellow fever furnishes a striking example of such hemorrhages. The changes in the bile are characterized by its increased viscosity, great increase in its pigment, and diminution of the bile acids. The parenchymatous changes in the liver are evidence of the action of the toxins on the liver. Similar changes occur in the kidneys. The urine is bile stained and the true

biliary pigments, notably urobilin, are greatly increased.

Five types of disease require differentiation from hemolytic icterus and, of course, from one another. The first is *pernicious anemia*, in a number of cases of which diagnosis has been difficult. Next is mentioned *Gilbert's familial cholemia*, regarded by some as identical with hemolytic icterus. Chalker, a recent writer, regards the former as a mild type of the latter, and points out well-marked dissimilarities. Third comes *Banti's disease*, including its hemolytic form. Fourth in order is *polyglobulia*, both of the compensatory and cyanotic types. Finally is added the Gaucher type of *splenomegaly*, because some of the recorded cases might have been termed hemolytic icterus. Mosse (Berl. klin. Woch., Apr. 14, 1913).

The special feature about hemolytic jaundice is the intensity of the jaundice in contrast to the fine state of the health in general. Roch (Revue méd. de la Suisse Romande, Mar. 20, 1914).

In many varieties the toxins that excite these changes are generated in the intestinal tract, as gastrointestinal symptoms are usually prominent in the initial stage of the illness. In this way we may account for the absence of specific organisms in the liver in acute yellow atrophy, for example. According to Hanot, the form of icterus gravis in which the bacillus coli is found is accompanied by lowering of the temperature, while the other forms of the same disease which are accompanied by fever are characterized by the presence in the liver and blood of pyogenic microbes.

Syphilitic jaundice, according to Werner, is characterized by (1) its appearance in the early secondary stage, (2) the presence of fresh specific manifestations, (3) the in-

fluence of treatment, and (4) its sudden development without gastric disturbance. Long duration is not characteristic of syphilitic jaundice. In typical cases this icterus occurs at a time when syphilis affects the skin and mucous membranes. Hepatic enlargement is not a striking feature in the disease. In 22 out of 50 cases the jaundice was noted within six months after the infection. The syphilis in most of Werner's cases was severe.

In some cases, as in pyemia and snake-venom, the poison finds its way to the liver through the general circulation.

Treatment.—A careful search for the causative toxic, whatever that may be, is the first step. Treatment aiming to **remove the cause**, often syphilis, malaria, and helminths, should then be supplemented by means calculated to **prevent hemolysis** and **stimulate regeneration of the blood**—arsenic, calcium chloride, **organotherapy**, or **cholesterin**. Iron has been praised by Widal, to stimulate the process of blood repair, **Rest** and **nourishing food** are indicated. **Splenectomy** has given particularly good results in familial hemolytic jaundice, often proving almost curative. Exposure to the **Röntgen rays** has also been recommended.

Of 12 out of 17 patients on whom **splenectomy** was performed by the writer, 10 are living; 9 are in excellent health without jaundice or anemia. There was 1 operative death. One patient died 4 months after operation; another patient with a severe form of the acquired type of the disease was in excellent health for 18 months, had a relapse after 2 years, and is again in fairly good health after 2½ years following two **transfusions**. Four patients have been in

excellent health for 14 months, 15 months, 23 months, and 5½ years respectively. Griffin (Surg., Gynec. and Obstet., Aug., 1917).

In a personal case, the patient and a brother had both had hemolytic jaundice since childhood and the spleen was extremely large. On exposure of the spleen to the X-rays, pains developed in the region, but after **splenectomy** both the pains and the jaundice disappeared in 2 days. Hartmann (Bull. de l'Acad. de méd., July 29, 1920).

Recovery obtained with **antigonococcus serum** in a woman of 30 with gonococcic septicemia and jaundice. Widal and May (Bull. Soc. méd. des hôp. de Paris, July 23, 1920).

Case of syphilitic jaundice in the early secondary stage, previously untreated, in which subsidence of jaundice and skin eruption occurred in 2 weeks under **mercury, rest, milk diet, and methenamin**. Ardin-Delteil, Derrien and Azoulay (Bull. Soc. méd. des hôp. de Paris, Feb. 3, 1922).

Iron and arsenic do not benefit much in these cases. In the variety associated with congenital syphilis, no cure of the jaundice is to be expected from antisyphilitic treatment, though general improvement may result. **Cholesterol** yields temporary improvement. The **X-rays** reduce the spleen, but the other signs persist. The best treatment is **splenectomy**. In the congenital type a cure may be predicted from this operation. In the acquired type, unless secondary to grave diseases such as cancer and cirrhosis, the prospects for cure are also excellent. **Blood transfusion** before and sometimes after the operation has greatly reduced the high early mortality. In cases with cholelithiasis, it is best to do splenectomy first, but if the patient's condition permits the stones may be removed at the same operation. Tileston (Medicine, Aug., 1922).

Report of 9 out of 10 cases of hemolytic jaundice cured by **splenectomy**, the remaining case succumbing to portal thrombosis. Gänsslen (Deut. Arch. f. klin. Med., Sept. 5, 1922).

Case of icterus, chiefly dynamic (non-obstructive), without acholia or bilirubinuria, in which an erythema dose of **X-rays over the spleen** resulted in recovery. Szemző (Deut. med. Woch., Oct. 13, 1922).

Case in which, when **splenectomy** was performed, 2 supernumerary spleens were found. One of these organs, 6 by 3 cm. in size, was left *in situ*. The jaundice promptly disappeared, *vis.*, in 3 days. The blood examination made 51 days after the operation showed, however, an increase in the white blood cells to 42,000. The polymorphonuclear cells were only 6.5 per cent., and the lymphocytes, 84 per cent. F. H. Bartlett and M. Wollstein (Amer. Jour. Dis. of Childr., Sept., 1924).

Two cases of hemolytic icterus in which **splenectomy** gave good results, maintained for 3 years and 1½ years, respectively, to date. Hannema (Lancet, Jan. 2, 1926).

Injection of **insulin and sugar** found beneficial in hepatic insufficiency, particularly when accompanied with grave jaundice. Jacoby (Deut. med. Woch., Jan. 8, 1926).

ICTERUS NEONATORUM (See NEWBORN, DISEASES OF).

ACUTE INFECTIOUS JAUNDICE.—In 1886 Weil described "A peculiar form of acute infectious disease characterized by jaundice, swelling of the spleen, and nephritis." This was recognized by German writers as a new disease—**Weil's disease**,—but others have looked upon it only as what has long been described as "acute infectious jaundice," a name that serves sufficiently to designate it.

During the World War many cases of infectious jaundice developed in Italy, France, Turkey, etc. At least one form of the disease was shown to be caused by the *Spirocheta* or *Leptospira icterohemorrhagiae* (or *Spirocheta icterogenes*). Hence the name **spirochetosis icterohemorrhagica** now

frequently given to this type of the disease.

The acute jaundice witnessed in the United States in small epidemics is obviously infectious, but the spirochete has only rarely been found in these cases, although some patients have presented hemorrhagic manifestations. The true spirochetel disease is a far more serious disorder than the common epidemic jaundice.

Symptoms.—The disease typically presents the symptoms attending acute infections generally. It sets in suddenly, usually with chill, followed by fever, pain in the back and limbs, loss of appetite, thirst, general malaise, headache, giddiness, and usually diarrhea. The symptoms increase for a day or two, the temperature rising rapidly to 104° or 105° F., weakness increases, and there is mild delirium. Jaundice appears on the second or third day, with marked enlargement and tenderness of the liver and swelling of the spleen. The urine becomes albuminous and shows the other signs of acute nephritis. There is marked derangement of the digestion—furred tongue, nausea, and sometimes vomiting. The symptoms begin gradually to subside by the fifth to the eighth day. The persistent high temperature falls, gradually reaching the normal by the tenth or twelfth day. The jaundice abates with the other symptoms.

From the hundreds of cases in the Italian army the writer had under his care, he describes the disease as follows: There is an incubation period of a week or two, then the stage of invasion, which lasts from 2 to 6 days, with fever usually so slight that it is not noted, and without jaundice, although there may be intense

muscular pains, suggesting rheumatism, or digestive disturbances with headache, suggesting typhoid. Then follows the stage of jaundice, during which the temperature drops to normal or even below and the pains subside. There is usually an interval of a day between defervescence and the onset of the cholemia. It is accompanied by weakness, at times extreme. The spleen and liver are enlarged. A special feature of the disease is that the temperature runs up again after an interval of from 4 to 6 days. The glands also swell, especially in the right axilla. There were no hemorrhages from skin or mucosa in his cases, but a tendency to epistaxis was common. Bravetta (Policlinico, May 26, 1918).

As already implied, it is evident, however, judging from the cases of infectious jaundice observed in different countries, that several types of the disease occur.

From a seacoast district in Denmark, Kamp and Wernoe have described a form of jaundice affecting both man and the domestic animals and in which bacteriologic examination has revealed only paratyphoid B bacilli. The disease is transmissible from man to animals and *vice versa*. The jaundice is the first symptom, with tenderness of the gall-bladder; but diarrhea, often bloody, with colicky pains, mainly around the umbilicus, persisting for weeks and months, is the most serious feature, along with great depression, somnolence, anemia, and dull, sunken eyes. Hemorrhages are common, and also complicating pneumonia and myocarditis. In surviving cases there seems to be a tendency to recurrence.

The type of case of epidemic jaundice witnessed in the United States is more usually of the form seen by Hiscock and O. F. Rogers (Jour. Amer. Med. Assoc., Feb. 18, 1922) among 69 students at Yale University. In these cases the symptoms included lassitude, anorexia, often headache, and in some cases chills, nausea, and pain in the side, back, or on lateral movements of the eyes. The stools were usually lacking in normal color. There were several examples

of transmission by close personal contact. The average interval between succeeding cases was 7.2 days. *All the cases recovered*, though in some cases the disease lasted 10 days to 3 weeks.

Convalescence is usually uninterrupted, but in a certain number—about one-fourth—the fever recurs within a week, lasting five or six days, in only a few cases being accompanied by recurrence of jaundice, swelling of the liver and spleen, and albuminuria.

Convalescence is always slow, strength not returning for many weeks.

Of the symptoms, the most marked usually are the muscular pains, especially in the calves of the legs. The pains may be so severe as to obscure the other symptoms. They are much increased by movement and by pressure on the muscles.

Etiology.—Spirochetal jaundice is met with mostly among adolescent or young adult males, but has been seen in children as young as 8. It occurs usually in the summer, affecting chiefly workmen engaged in insanitary occupations or environments. It is uncommon in America. During the war, the disease seemed to be communicated by field rats which infested the trenches, and to enter through abrasions. According to Uhlenhuth and Zülzer, a primary infection from water is not impossible.

Epidemics of Weil's disease contracted in swimming-pools have been reported.

The cause of the milder forms of infectious jaundice met with in the United States is unknown.

Infectious jaundice, according to G. Blumer (Jour. Amer. Med. Assoc., Aug. 4, 1923), may assume family, institutional, city, country and state-wide types. In city outbreaks, only certain sections may be attacked, or the distribution may be wide-

spread. Once a district is infected, the disease may be looked for annually. It is essentially a seasonal disease, 72 per cent. of 50 outbreaks having occurred during the fall and winter. It is a disease of childhood and adolescence. The sexes appear equally susceptible. There is almost unanimous agreement that personal contact is the usual method of transmission, but the exciting agent has never been demonstrated. Large outbreaks should make the diagnosis a simple matter, although in the South the disease might possibly be confused with yellow fever. Dengue might also be thought of, as the muscle pains may be very severe. The complete absence of fatalities in most outbreaks is a striking feature.

Two cases of jaundice with spirochetes, believed to have been the first cases to be recognized in the vicinity of Philadelphia. J. Sailer (Amer. Jour. Med. Sci., Sept., 1925).

Morbid Anatomy.—In the more severe cases the liver changes resemble those found in acute yellow atrophy, but much less pronounced. There are fatty degeneration and cloudy swelling of the renal epithelium, or even an acute parenchymatous nephritis. Minute hemorrhages exist in various organs and on the serous surfaces. The spleen is enlarged. There are no traces of typhoid ulceration. Where the spirochete causes the disease, it may usually be found in the urine.

Prognosis.—Spirochetal jaundice sometimes terminates fatally. In the commoner epidemic jaundice of unknown etiology, the prognosis is uniformly favorable.

Treatment.—This is usually symptomatic. The pains require anodynes for their relief. **Arsphenamin** and **serums** have been given with asserted benefit in the spirochetal cases.

In 14 cases of infectious jaundice the treatment adopted in most cases was **calomel** or **mercury with chalk**, **salines**, and, if necessary, **enemata**, and then **salicylates**, and liquid ex-

tract of *cascara*. Whitaker (Brit. Med. Jour., Oct. 14, 1911).

In many cases of acute infectious jaundice in children it is only necessary to restrict fats and to give soup, lean meat, vegetables, skimmed milk and bread. C. Herrman (Med. Rec., Aug. 30, 1913).

In 300 cases of spirochetal jaundice, a combination of arsenic and mercury proved very useful. Carpi (Policlinico, July 29, 1917).

Active catharsis is not indicated, but rather intestinal antiseptics and symptomatic treatment. Chloroform water proved satisfactory for vomiting and camphorated tincture of opium for pain, followed by ferruginous tonics during convalescence. Waters (Jour. Amer. Med. Assoc., Oct. 28, 1922).

Mada has advised intravenous injection of serum from convalescent patients or immunized horses. Arspenamin and neoarsphenamin have also been found useful. Parmanand (Indian Med. Gaz., Feb., 1922).

The mortality of 57.1 per cent. in severe cases was reduced by serum treatment to 34.7 per cent. In severe cases in patients under 40 years of age treated within 6 or 7 days after onset, the mortality was reduced to 13 per cent. The author prefers intravenous treatment. In slight or moderate cases, 20 c.c. of serum suffice. The serum markedly reduces hemorrhages and abscess formation and improves the pulse, temperature, and jaundice. By way of prophylaxis he advocates treatment of the soil with lime nitrogen fertilizer, extermination of rats, and improved drainage of mines. Mada (Japan Med. World, July, 1922).

ACUTE YELLOW ATROPHY OF THE LIVER (MALIGNANT JAUNDICE; Acute Parenchymatous Hepatitis).—**Definition.**—A grave form of jaundice characterized by extensive destruction of the liver cells with atrophy of the liver, and clinically by grave constitutional disturbance in which the cerebral symptoms are especially prominent.

Symptoms.—In the prodromal period there is no time to distinguish it from ordinary jaundice. The same symptoms usher in loss of appetite, malaise, nausea, and vomiting, jaundice following a day or two. It differs from ordinary jaundice in the occurrence of some rise of temperature.

This stage may last from a few days to two or three weeks. The bowels are constipated and feces pale; the urine contains bile pigment. There may be pain in the hepatic region.

Suddenly a marked change occurs, characterized by severe headache, repeated vomiting, delirium, and restlessness. The vomited matters are at first bile stained and later contain blood more or less altered, and the stools may also contain blood, making them dark and offensive. At the same time the jaundice deepens and becomes of a greenish hue. The temperature falls to normal, or usually below it; the pulse rises to 120 or more and becomes weak. Stupor and coma develop. There may be convulsions. In women menorrhagia may occur and, if pregnant, abortion or premature delivery takes place.

The urine becomes deeply bile stained and often contains tube casts. It becomes lessened and may be suppressed. There is great diminution, or even absence, of urea, and its place usually is taken by abnormal constituents, especially by tyrosin and leucin.

The most characteristic physical sign in this stage is the rapid diminution, it may be disappearance, of the area of hepatic dullness; so that the hepatic area may become tympanitic. It is also frequently tender, even during coma.

This stage lasts only 2 or 3 days and nearly always ends fatally.

Diagnosis.—It is not possible to distinguish acute yellow atrophy before

the development of the grave symptoms. Then the symptom group is characteristic: intense jaundice; severe, persistent vomiting; rapid disappearance of hepatic dullness; delirium, passing rapidly into coma; leucin and tyrosin crystals in the urine.

Hypertrophic cirrhosis sometimes presents similar symptoms, but the long duration and the large liver serve to exclude this affection. In this the symptoms of icterus gravis may develop and the case present all the features of acute yellow atrophy.

Phosphorus poisoning closely resembles acute yellow atrophy, but the liver does not diminish so rapidly, if at all, the nervous symptoms are not so grave, leucin and tyrosin do not usually appear in the urine in phosphorus poisoning, and the gastric symptoms are usually more severe.

Etiology.—This disease is rare. A few observers have, however, seen several cases within a few months, indicating an endemic agent, while others with large experience have not met a case.

No age is exempt, from the infant of a few days to the octogenarian. It is most common between the ages of 20 and 30 years.

It is more common in females than males, especially between the ages of 20 and 40; that is, during the child-bearing period. Pregnancy has a most important bearing on the causation, nearly half the cases met with in women occurring during pregnancy, especially the latter part of it. This is probably explained by the fact that some degeneration of the cells of the liver and kidney is a common condition in pregnancy. Fear and mental emotion have apparently been the cause in a few cases.

In cases in which he was in doubt as to the diagnosis between cholangitis and acute and subacute atrophy of the liver, the writer operated and, although finding an atrophic condition, established **drainage of the hepatic duct**. In some cases marked improvement followed, bile flow increased, and the patients recovered. W. Braun (Berl. klin. Woch., Dec. 16, 1922).

Case of malignant secondary syphilis in a young married woman, with deep jaundice. At necropsy, typical acute liver atrophy was found. No anti-syphilitic drugs had been given. Erasmi (Derm. Zeit., Oct., 1925).

Alcoholic excess has preceded the disease in several cases. The disease may be the result of various infections, such as typhoid, diphtheria, and septicemia. The resemblances of the symptoms to those of phosphorus poisoning are undoubted, but there are essential differences in the resulting morbid changes that render it clear that the two conditions are not identical. In view of the variety of conditions under which the disease occurs, it is highly probable that it is due to various forms of infection.

Case of acute yellow atrophy of the liver in a previously healthy man five months after infection with apparently mild syphilis. The liver infection proved fatal in ten days. In this and 3 other cases recently reported, search for spirochetes in the liver was unsuccessful. The affection is probably of toxic origin. Acute yellow atrophy of the liver in connection with syphilis has been observed in about 50 recorded cases. W. Fischer (Berl. klin. Woch., May 11, 1908).

Morbid Anatomy.—The liver is greatly reduced in size; it may be less than half its normal weight. It is thin, flabby, and wrinkled in appearance.

On section it is tough rather than firm. The cut surface varies in color

from a yellowish to a reddish brown and is often mottled irregularly. The lobules are small and indistinct; in the parts most advanced in degeneration they cannot be distinguished.

On microscopical examination the liver cells are found greatly degenerated, containing swelled, indistinct nuclei and fat granules. In many parts they have been entirely replaced by fat granules and *débris* held together by the liver stroma.

In less degenerated parts the periphery of the lobules is most affected where the cells are disintegrated and the biliary canaliculi distended with desquamated epithelium and granular masses of bile pigment, constituting a complete obstruction to the flow of bile. In these parts active cell division may be found, as if an effort were being made to regenerate the hepatic parenchyma. It is possibly due to this activity that recovery takes place in rare cases.

In acute yellow atrophy, the poison, whatever its nature may be, may affect the liver very unequally and in different degree. The poison may also act only locally, and recovery take place. Stroebe (Ziegler's *Beiträge*, vol. xvii, p. 206).

The larger bile-ducts are usually free from bile, containing mucus only; the gall-bladder often contains a little bile.

Micro-organisms of various kinds have been found in some cases, but not with such constancy as to indicate that they have taken any active part in the causation of the disease.

Prof. A. B. Macallum, from a study of a case of mine, and others concluded that the disease was caused by a toxic agent carried to the liver by the portal vein and, therefore, originating in the intestine.

There is general bile staining of other organs and tissues. Numerous hemorrhages are found in various situations. The heart, voluntary muscles, and renal epithelium usually show fatty degeneration. The spleen is large and there may be considerable effusion into the pleural and pericardial cavities. There are evidences of catarrh in the digestive tract.

In acute yellow atrophy the cord may show changes which seem to be, like atrophy of the liver, the result of the severe general intoxication (Goldscheider and Moxter).

Prognosis.—The disease is so fatal that recovery almost implies a mistake in diagnosis. Yet Martinez states that the statistics of the Havana Civil Hospital show that acute yellow atrophy is by no means necessarily fatal. Weising, in 1892, in reporting a favorable case, stated that it was the sixteenth on record at the time.

Treatment.—This is purely symptomatic. There are no remedies known to have any influence on the disease. On the plea that the hepatic lesions are due to autolysis, Sajous advocates **saline solution**, used freely by the mouth, rectum, hypodermically, or intravenously, as soon as the nature of the disease is recognized. The rectal injection of **peptone**, **eggs**, and **milk** to nourish the patient, while avoiding the hepatic circuit, was a feature of Weising's successful case. The **ice bag** over the liver affords relief.

In a case of acute yellow atrophy sole dependence was placed on hypodermic **sodium bicarbonate injections**. One week after admission to the hospital the patient began to improve, the liver dullness rapidly receding, and was well in 1 month. C. P. Longridge (*Jour. Royal Army Med. Corps; Med. Rec.*, Oct. 7, 1916).

ABSCESS OF THE LIVER (Suppurative Hepatitis).—Symptoms.

The outset of the disease is always insidious and the course may be latent throughout, an unsuspected abscess being found at the autopsy. When not latent, the cardinal symptoms are: fever, with free perspiration, pain, enlargement of the liver, and signs of septic infection. There are loss of appetite, more or less rapid emaciation and increasing weakness and anemia. There is a sense of weight and distress in the epigastric and right hypochondriac regions, with sometimes hiccough, nausea, and even vomiting. An icteroid hue develops; rarely, marked jaundice. The temperature is elevated from the first and is of a septic character. It is irregular, being normal at times, then rising to 103° F. or more, with a more or less marked chill, to defervesce again with profuse sweating. These variations may be so regular as to clearly simulate malarial fever, but the variations lose their regularity in a few days. In other cases typhoid fever is simulated. With the evacuation of the pus, the temperature may fall to normal and remain so; much will depend on the thickness of the abscess wall and whether other foci of suppuration coexist. The pulse rate varies in general with the temperature, but toward the end of life it becomes greatly accelerated and feeble.

Pain is variable, and probably is not present until the abscess approaches the surface of the liver. It is usually referred to the scapular region, but may be felt in the region of the liver. The patient usually finds lying on the back or right side most comfortable; on the left side the liver drags on its liga-

ments and any inflammatory adhesions that may be formed and causes discomfort. Pressure at the costal margin, especially in the nipple line, is usually painful.

Enlargement of the liver is most marked in the right lobe, and may be more apparent in the erect posture. In multiple abscesses and pyelephlebitis the enlargement is general and rarely great. In tropical abscess when situated, as it usually is, in the dome of the liver, the enlargement is chiefly upward, contrasting with the downward enlargement usual in new growths of the liver. The area of thoracic dullness may be sharply convex upward and rise to the fifth rib in the midaxillary line and posteriorly to the angle of the scapula. It has been reported to even reach the second rib in front and the spine of the scapula behind. In these cases of extremely large abscess the right side is bulged and the lower margin of the liver depressed, it may be, to the iliac crest; over the liver there is tenderness and often crepitus on palpation; and occasionally fluctuation may be elicited.

According to Giordano, important features leading to the diagnosis of abscess of the liver are apparent inflammation of the pleura with possible effusion, and a very tender spot, when these findings accompany the classic symptoms of hepatic abscess.

Deep-seated pain in the region of the abscess, elicited by a sudden thrust with the end of the finger, is a practically constant sign of liver abscess. The writer usually begins with the left side, to accustom the patient to the maneuver. A. I. Ludlow (*Surg., Gyn. and Obst., Mar., 1923*).

Owing to the frequent situation of the abscess in the dome of the liver, implication of the lung is more frequent

in the tropical, or amebic, cases than in the septic ones occurring in our northern climates. The pulmonary symptoms often occur early and become so pronounced as to obscure the hepatic symptoms. They usually consist of a stitch-like pain and signs of exudation into the pleura in the right axillary region, dyspnea, and hacking cough with little expectoration. Later, when the abscess discharges into the bronchi, severe paroxysmal cough develops, with abundant expectoration, often greatly increased on lying down. The sputum consists of a "dirty-red or brownish puriform matter. There is no matter like it expectorated in any disease of the lung itself, and I believe that its appearance is pathognomonic of abscess of the liver, or, at least, of abscess perforating the lung" (Budd).

Flexner reported a case, probably the only one in literature in which secondary perforation of the inferior vena cava resulted.

A slight degree of jaundice is not rare; it may vary with the variations of temperature. Exceptionally more marked and prolonged jaundice is caused by pressure of the abscess on the common bile-duct. Ascites may result in a similar manner from pressure on the portal vein.

Case of abscess of the liver in connection with pregnancy. The abscess was a single large one in all but 1 of the 5 cases. Both of the women survived in the 2 cases in which an operation was done. The main point in such cases is to bear in mind the possibility of an abscess of the liver when confronted with puzzling symptoms during or soon after a pregnancy. In the 5 cases reported the diagnosis was presumptive in 1 case, confirmed by the operation; in another case the diagnosis had been positive, but in the 3 other cases

pleurisy or pleuropneumonia had been diagnosed. Chavannoz and Loubat (*Revue de gynäk.*, Dec., 1911).

Diagnosis.—As the suppurative process in the liver may be latent, it is often impossible to make a diagnosis of hepatic abscess, especially in the early stage.

The occurrence of pain in the right hypochondrium or in the scapular region, some enlargement and tenderness of the liver, and irregular fever, usually with chills more or less marked, in a case with a history of ulcerative processes anywhere in the digestive tract afford fairly certain grounds for a diagnosis.

Bertrand called attention to perihepatic friction in suppurating hepatitis as a diagnostic sign that may be perceived both by ear and hand, and precedes by several days edema of the parts.

If discharge takes place through the lung the character of the pus may be sufficient to establish the diagnosis; especially if ameba found in it, otherwise abscess of the lung or empyema will have to be excluded.

Perforation externally may render diagnosis easy. If the abscess is in the liver the needle inserted into it will move with the respiratory movements of the liver unless adhesions be so firm that the liver is quite fixed. Empyema of the gall-bladder would, of course, move with the liver, as might also an abscess adherent to the under surface of the liver.

Attacks of gall-stone colic with marked intermittent fever often closely simulate hepatic abscess. In the gall-stone cases the attacks of fever are paroxysmal, with severe pain and sweating. The attacks may recur with great regularity. In the intervals between

the attacks there is complete apyrexia, and the general nutrition is well maintained. Such a history may be continued for years.

As abscess of the liver is a secondary affection, the previous history is important. The primary disease may be dysentery, ulcer of the stomach, hemorrhoids, rectal ulcers, appendicitis, etc.

X-ray examination may give more information than the symptoms. Permitting of change of position of the patient, fluoroscopy proves superior to the X-ray plate for the localization of the abscess.

The greatest obstacle to the diagnosis at present is the lack of appreciation that amebic abscess is one of the common maladies. The clinical picture, however, is rarely complete. Fever, of varying type, is one of the earliest and most constant signs. Pain was noted in 16 of the writer's 19 cases. The pain may be steady or intermittently sharp. Diaphragmatic involvement causes a dry cough and at times singultus. Allan (*Archives of Diag.*, July, 1917).

Pylephlebitis is now sometimes spoken of as synonymous with pyemic abscesses of the liver. This may be true in case of multiple abscesses, but not in single abscesses. There may be a localized or a diffuse pylephlebitis without a liver abscess, or either of these with a single or with multiple abscesses, or a liver abscess with no demonstrable pylephlebitis. Among 2237 cases of operated acute appendicitis there occurred 3 instances of hepatic abscess, or 0.13 per cent. A chill just after operation points to a rapid infection of the portal system, usually with resulting profuse pylephlebitis and multiple liver abscesses. Where, after the usual postoperative gradual drop of temperature for 3 or 4 days, there is a rise to 101° to 102° 5 to 8 days later with a chilly sensation, a circumscribed venous infection or thrombosis leading to septic embolism in the liver may be suspected; in

this type there is often only a single abscess, and recovery follows its evacuation. Continuous fever with repeated chills and a temperature of 104° or 105° suggests pylephlebitis and multiple liver abscesses. In all of the writer's 10 cases there was marked leucocytosis with polymorphonuclear increase. Pain is not a constant symptom. Jaundice is almost invariably present and appears early. Tenderness can always be elicited by the fist percussion of Murphy. Lassitude and anorexia are suggestive. A firm or boggy edema over the region of the lower ribs in the midaxillary line, usually with dilated veins over the lower chest and upper abdomen, is a valuable diagnostic sign.

In 10 cases X-ray examination was negative in only 2. The other 8 showed elevation of the right side of the diaphragm and sometimes restriction of movement on the same side. In 3 there was also a shadow in the lower right chest, interpreted as fluid; this occurred only where the abscess or abscesses affected the upper surface of the liver. In practically all the cases the clinical diagnosis at first was a basal pneumonia or subdiaphragmatic abscess; in all, however, the proper diagnosis of liver abscess was made before operation. E. L. Eliason (*Surg., Gyn. and Obst.*, Apr., 1926).

The existence of leucocytosis may prove of importance as indicative of suppuration. The diagnosis may sometimes be established by aspiration: an operation that may be resorted to without any great degree of danger. Of course, failure to find pus does not negate the existence of abscess, as the needle may not reach it or the contents may be too thick to enter the needle. The patient should be anesthetized, as many punctures may be required. The needle should be inserted in the lowest interspace in the anterior axillary line, in the seventh interspace in the mid-axillary line, or in the center of the dull

area behind. The Mayos advise against exploratory aspiration until all necessary preparations have been made for immediately opening and draining the cavity.

Etiology.—Abscess of the liver results occasionally from traumatism, as from a blow or a punctured wound.

Abscess of the liver, according to Oddo, is a rare condition in children, except as the result of injury. Sometimes the abscess develops immediately after the injury, while at other times a latent period intervenes. Generally the injury has been applied directly over the hepatic region, in which case the abscess is primary. In the occasional abscesses resulting from an injury to some other part of the abdomen, abscesses are secondary or indirect. The symptoms of a traumatic abscess of the liver are local pain, swelling, and fluctuation; at the same time there is fever, either remittent or continuous, with rapid and profound cachexia in every case. The natural tendency of the liver abscess is to rupture, either through the skin or through the respiratory passages. The evacuation is followed generally by a rapid amelioration, but in every case surgical intervention brings about a more certain and rapid cure.

Six cases of liver abscess. One was due to mechanical injury, indirectly causing a contusion of the liver, and thus furnishing a point of lessened resistance to the action of bacteria. The second was due to the direct extension of the infection from a suppurating and gangrenous gall-bladder, the abscess being formed on the under surface of the liver. Two cases were due to dysentery. In 1 case autopsy confirmed the presence of the etiological factor. In 2 cases no definite etiological factor could be assigned. Jacoby (Med. Rec., April 11, 1914).

Apart from traumatism, the two chief avenues by which bacteria gain access to the liver and excite suppuration are the portal vein and the bile-ducts. Of these, the portal vein is the

chief one, as it may convey germs from any part of the digestive tract; hence the frequency with which abscess of the liver follows ulcerating lesions of the intestines, as dysentery, appendicitis, typhoid fever, hemorrhoids and other rectal diseases. The formation of gall-stones has been regarded as the most frequent cause of liver abscess in Germany, according to Korte. Covert witnessed a case in which the abscess gave passage to 30 gall-stones.

Emboli from these sources may excite suppurative pyelophlebitis, from which abscesses may result by extension into the liver substance.

Case of a physician aged 68 who had had 2 severe attacks of gall-stone colic. At operation a perforation of the gall-bladder, with pus issuing, was found, with an abscess of the size of an egg at the junction of the cystic and common ducts. Upon the under surface of the right lobe of the liver was a mass as large as a lemon. A tube was inserted in the gall-bladder, a Penrose drain in the abscess, and a needle in the liver abscess for diagnostic aspiration. The liver pus yielded a pure culture of *B. aerogenes capsulatus*, the gall-bladder a mixed infection. The liver abscess was **incised, drained and irrigated** twice daily with **Dakin's solution**. Recovery followed, but symptoms of malignancy developed 16 months later and death occurred. The infection of the liver in such cases is by invasion from the intestinal tract, where gall-bladder tissue is already lowered in resistance from previous infections. C. C. Snyder (Surg., Gyn. and Obst., May, 1924).

Infective processes in the umbilical cord in infants may extend along the vein to the liver and produce one or more abscesses. In a similar manner they may result from abscess of the spleen.

In general pyemia abscess of the liver is rare, as the germs have to pass

through the lungs to reach the liver. Suppurative wounds of the head are, however, followed by hepatic abscess with comparative frequency. It may possibly happen in these cases that the infective agent reaches the hepatic veins by "retrogressive embolism" from the vena cava.

Next to the portal vein, the most common avenue of invasion of the liver by pyogenic organisms is the bile-duct. The germs originate in the intestine, and the inflammation resulting from their presence in the duct is probably always preceded by injury, usually from pressure of a gall-stone, more rarely from the irritation of a parasite or a foreign body, such as a pin, as was the case in an instance reported by Lambert.

Chronic abdominal infection may cause types of hepatitis which render the patient invalid even after successful surgical intervention. An infection once initiated within the abdomen, its course is chronic and the liver reacts in various ways, but always with some degree of degeneration. Heyd, MacNeal and Killian (*Amer. Jour. of Obst. and Gyn.*, Apr., 1924).

Case of ascarid abscess in the liver. There was no history of gall-stones, but ascariasis dated back to childhood. The pus contained a long ascarid, colon bacilli and pneumococci. The patient, a multiparous woman, recovered after the evacuation of the abscess. Erb (*Deut. Zeit. f. Chir.*, May, 1925).

In tropical climates there is close association between abscess of the liver and dysentery: an association explained by the presence in both of the dysentery ameba.

Morbid Anatomy.—In septic cases the abscesses are usually multiple and irregularly distributed throughout both lobes. Traumatism may give rise to a solitary abscess, and such may also result from a single embolus. The

liver is usually uniformly enlarged. Its surface may present no abnormal appearance. In many cases, however, there are yellowish points showing beneath the capsule. On section isolated pockets of pus are found, varying in size from a small point up to 3 or 4 mm. or more in diameter, the larger ones being probably formed by the coalescence of two or more smaller abscesses. Many are dendritic in form, and on examination are found to communicate with the portal vein, being doubtless formed by suppuration of its branches. The walls of the abscesses are shreddy, especially in the larger ones, and the cavity may be divided by many trabeculæ. The contents vary according to the age of the abscess and the nature of the infective agent: they may be thick and viscid; or fetid, bile stained, and containing masses of necrotic tissue; or the pus may be thick and "laudable." All the branches of the portal vein in the liver may be involved, but sometimes thrombi circumscribe the infection and preserve sections of the liver from invasion. The suppurative process may extend backward even into the gastric and mesenteric veins.

Metastatic abscess of the liver, when of pyogenic origin, may assume one of 2 types: (1) Liver pyemia or a septic pylephlebitis of the branches of the portal vein, secondary to emboli coming from the mesenteric veins, and due most often to gangrenous appendicitis. The abscesses are multiple and consist of narrow suppurating and necrotic tracts frequenting the branches of the portal vein; efforts to evacuate them are generally useless owing to their multiplicity. (2) Abscesses arising from infective processes in the alimentary canal and its associated organs. This type is also seen after severe trauma to the liver, after ulceration due to foreign bodies, or from general pyemia. Such abscesses are solitary

and should be operated on as soon as they are localized.

The writer reports a case of hepatic abscess in a child of 4 years. It was of pyemic type, and recovery followed operation. The successful outcome is ascribed to the fact that the abscess was solitary and was not pylephlebitic. *Streptococcus hemolyticus* was found in both the liver abscess and the appendix. J. A. Cahill, Jr. (Internat. Clin., iv, 234, 1922).

If infection has taken place through the bile-ducts, obstruction by gall-stones usually exists and the gall-bladder and the bile-ducts generally may be dilated and full of pus, often bile stained.

Very large abscesses may result from suppuration around echinococcal cysts; their nature is indicated by the presence of portions of the cysts.

Tropical (Amoebic) Abscess.—There may be one or more; in the latter case there is usually one larger than the others. They may vary in size from a few millimeters in diameter up to an orange or even to a child's head. The larger abscesses usually occupy the right lobe, being situated, as a rule, at the under surface above the hepatic flexure of the colon or in the dome of the liver (Lafleur). In Waring's statistics of 300 cases, in 62 per cent. there was only a single abscess. The small multiple abscesses are usually superficial. In the smaller abscesses, being more recent, the walls are shreddy and not sharply defined from the contiguous inflamed liver substance. Their contents vary from a yellowish gray to a reddish brown (due to the presence of blood), and often contain shreds of necrotic liver tissue. In old abscesses the walls are firm, thick, and fibrous. The contents of all the abscesses are chiefly remarkable for the small number of leucocytes that are present.

When the abscess reaches the surface it may rupture and pus escape into the peritoneal cavity, or, adhesions having previously formed, the pus may penetrate in any direction. It may discharge into the stomach, the intestine, the pelvis of the right kidney, or through the diaphragm into the pleural or pericardial sac. Adhesion of the lung to the diaphragm usually precedes its advent in this direction, and then the lung is invaded, an abscess forming and discharging into the bronchi. It may also perforate the thoracic wall and appear beneath the skin.

The large amoebic abscess of the liver is formed from multiple small abscesses developing in the branches of the portal vein, followed by extension of the inflammation to the liver parenchyma, coalescence, and development in concentric circles. The multiple small abscesses are usually overshadowed by the primary acute sloughing dysentery, and are not easily diagnosed nor treated. Sir L. Rogers (Brit. Med. Jour., Feb. 11, 1922).

Amoebic abscesses may be acute or chronic. The acute, which may be multiple, usually arise during or after acute dysentery, but occasionally in latent amoebic infection. With the usual symptoms of acute liver abscess there is generally some spasm of the abdominal muscles on the affected side, with marked tenderness on percussion. Since we have learned to recognize the small forms of the amoeba, it has been possible to find the parasite in every case, although occasionally only after repeated examinations. The chronic abscesses are insidious and most often afebrile, or nearly so. There is no marked leucocytosis, and the pain and tenderness are less marked. Often the enlargement of the liver is enormous. Where the abscess ruptures into the lung there is cough and expectoration of typical liver-abscess pus. R. W. Runyan and A. B. Herrick (Proc. Internat. Conf. on Health Probl. in Trop. Amer., 1924).

Prognosis.—Suppurative hepatitis is a grave disease, the mortality being over 50 per cent. In rare cases of single small abscesses and of mild pylephlebitis recovery possibly takes place by absorption or inspissation and calcification of the pus. There is, however, room for doubt as to the diagnosis of such cases. Multiple small abscesses are almost necessarily fatal, as they can rarely be evacuated either by natural processes or by surgical intervention. In large abscesses the mortality has been greatly reduced of late by the greater fearlessness and thoroughness with which they are operated on. Operation has seemed to give better results in the ordinary septic abscesses than in the amebic variety. The prognosis of amebic abscess has, however, greatly improved since the introduction of the treatment by emetine.

Treatment.—Apart from surgical means, little can be done, beyond relieving symptoms and maintaining the patient's strength until the abscess discharges spontaneously. Pain and cough are the chief symptoms to be relieved. In cases of rupture into the bronchi, cough is necessary for the removal of the pus, and should not be interfered with unless excessive.

In general, the treatment of a localized abscess of the liver consists of **incision, evacuation and drainage.**

In 12 cases of liver abscess and 2 of pylephlebitis following operated acute appendicitis, the treatment was uniformly **operation.** The 7 solitary abscesses were approached through the chest. Under local anesthesia the abscess was found with the needle. The rib, usually the 10th in the midaxillary line, was resected, with the needle still in place. The diaphragm was sutured in some instances and in others packing was placed against the pleura. The needle was then withdrawn and the

patient sent back to bed. Next day a needle was again inserted and when pus was located the **actual cautery** was slid along the needle until an opening was burned in the abscess cavity. The latter was then drained with a tube. In the remaining 7 cases, **laparotomy** was performed. The writer regards operation through the diaphragm as the treatment of choice. Of the 14 cases, 7 recovered. Adding these cases to 53 others in the literature, an average mortality of 54.5 per cent. was found. E. L. Eliason (Surg., Gyn. and Obst., Apr., 1926).

Ipecacuanha and particularly **emetine hydrochloride** are useful to prevent the development of amebic abscesses and may prove curative even when the latter have formed, especially if **aspiration and drainage** can be carried on at the same time. According to Rogers, prevention of the development of abscess from an amebic hepatitis calls for a daily dose of 30 to 60 grains (2 to 4 Gm.) of ipecac in freshly made pills or bolus, to be continued for at least 2 weeks, but at increasing intervals. No food or drink should be taken for several hours before and after each dose, which is best given in the evening. Vomiting must not be produced.

Case of a large amebic abscess of the liver that after about a year perforated into a bronchus. When the emetine treatment was begun the patient had been for five months raising a considerable amount of reddish pus, averaging each day from 200 to 250 c.c., and during this time had become emaciated and septic. At the same time there was some ulceration in the rectum. The X-ray examination showed an opacity at the base of the right lung merging with the shadow of the liver. The patient was thereupon given 6 injections of **emetine hydrochloride**, each 0.04 Gm. ($\frac{1}{4}$ grain), during a period of five days. The

injections were practically painless and produced no local induration. The expectoration was reduced to but a slight amount on the fifth day of the treatment, and after that it stopped entirely. The temperature fell to normal and the leucocyte count dropped from 49,000 to 19,800, and the polynuclear from 77 to 63 per cent. The ulceration in the rectum healed and subsequent X-ray examinations showed that the base of the right lung had cleared up. The patient improved markedly in general health and increased in weight 13 pounds. This experience with the clinical results reported by others demonstrates that emetine is a specific for amebic disease like quinine for malaria. Chauffard (Bull. de l'Acad. d. Méd., vol. lxxvii, p. 122, 1913).

Where **aspirating apparatus** are not available, as sometimes happens in outpost hospitals, the **abscess** can be **emptied by means of a large trocar and cannula**, and the cavity then irrigated with **saline solution**, to which has been added, on the last two occasions, a fluidram (4 c.c.) of **tincture of iodine** to the pint. Four fluid-ounces (120 c.c.) of a 10 grain to the fluidounce (0.65 Gm. to 1 c.c.) solution of **quinine bihydrochloride** were injected after each of 4 operations in a personal case, and the opening in the skin and deeper tissues closed by a single stitch. Powdered **ippecacuanha** was given by mouth in 30-grain (2 Gm.) doses at first, and in smaller quantities toward the end. The patient was discharged cured on the forty-second day, and there has been no recurrence. The procedure described can be done under **local anesthesia**. **Emetine hydrochloride** should now be on hand in every dispensary, both for treatment of acute and chronic amebic dysentery and for use in amebic hepatitis and liver abscess. L. G. Fink (Jour. of Trop. Med. and Hyg., Nov., 1912).

Of 35 patients with liver abscess treated by the writer with **ippecacuanha**, 21 were **only aspirated**: of

these, 17 were cured and 4 died. Five patients were treated by **aspiration** followed by **drainage**; of these, 3 were cured and 2 died. Nine were treated by drainage alone; among them 5 were cured and 4 died. The results are therefore largely in favor of aspiration alone. Of 32 patients treated with **emetine**, 27 were subjected to aspiration alone; of these, 20 recovered and 7 died; 2 were dealt with by aspiration followed by drainage; 1 patient was cured, the other died. Patients treated by drainage alone were 3; of these all recovered; these were all abnormal cases. Adding together these two series of cases, we get for aspiration alone a total of 48 cases, of which 37 patients were cured and 11 died, *i.e.*, a percentage mortality of 23. For aspiration, plus drainage, 7 cases, with a mortality of 3, *i.e.*, 43 per cent. Of 12 cases treated by drainage alone, 4 died, a mortality of 33 per cent., a verdict very much in favor of aspiration alone. Thurston (Indian Med. Gaz., March, 1914).

In multiple abscesses and in suppurative pyelephlebitis surgical measures are useless unless to open an abscess threatening to rupture. In single abscesses operation may promise fair success, especially in the non-amebic cases. In cases in which the abscess is discharging through the lung operation should be deferred if the patient's condition is favorable, as some recover spontaneously.

While Dieulafoy had stated that infection of the liver from acute appendicitis is always fatal, Quénu and Mathieu found 14 cases in which the infectious focus was single or there were but a few foci, and in which **operative measures** cured 12 of the patients. The operation was done through the pleura in 8 cases, generally on account of a vomica or because the tumor pushed up the diaphragm. Three personal cases described in detail included a man of 32, a woman of 36 (syphilitic), and a child over 10. All were in good health years after the operation.

Case of complete cure of amebic abscess by 3 series of 5 injections of 0.08

Gm. ($1\frac{1}{4}$ grains) of **emetine**. Lenoble and Jegat (Bull. Soc. méd. des hôp. de Paris, Apr. 13, 1922).

Cure of a case of amebic hepatitis with an 11- to 12- day febrile cycle of 4 months' standing by injections of 0.04 Gm. of emetine. Laporte and Roques (Bull. Soc. méd. des hôp. de Paris, Apr. 13, 1922).

Report of 15 cases without a death nor any untoward symptoms after **aspiration**, combined with medicinal treatment. An ordinary Potain's aspirator was used, but the needle was not inserted beyond $3\frac{3}{4}$ inches. When pus was struck, complete evacuation of the abscess cavity was at once carried out. If the pus proved too thick for aspiration, Manson's trocar and cannula was inserted along the tract of the aspiration needle and free evacuation thereby obtained. Manson-Bahr, G. C. Low, J. J. Pratt and A. L. Gregg (Lancet, May 12, 1923).

Recovery after **emetine** in amebic abscesses, using a large dosage, *viz.*, 0.03 Gm. ($\frac{1}{2}$ grain) subcutaneously 4 times daily for 3 or 4 days. Ciotola (Policlin., Dec. 17, 1923).

Recovery from hepatitis with amebic liver abscess obtained by means of **emetine enemas**. About 4 hours after a cleansing enema with pure water, the author injected 0.03 to 0.05 Gm. ($\frac{1}{2}$ to $\frac{3}{4}$ grain) of emetine in 100 c.c. ($3\frac{1}{2}$ ounces) of a mucilaginous solution, with addition of 20 to 30 drops of **tincture of opium**. Pappalardo (Rif. med., Nov. 3, 1924).

In 100 cases of amebic liver abscess treated by open operation the writer had a mortality of but 10 per cent. In the last 40 cases, wherever the patient's condition permitted delay, 0.06 Gm. of **emetine** was injected subcutaneously daily for 2 to 4 days before operation and for 4 to 7 days after operation. The author has also tried the treatment by **aspiration**. In this method the site of election for puncture is the point of greatest tenderness and swelling, often in the 9th interspace in the anterior axillary line. The needle should not enter more than 3 or at most 4 inches. As soon as the pus is

struck a small trocar is inserted under local anesthesia. A small skin incision facilitates this—a desirable feature, as a thin-walled abscess may be ruptured by the use of much force. A 30-c.c. (1-ounce) glass syringe connected with the trocar by a short, stiff rubber tube makes a satisfactory aspirator. If the pus is thick or the syringe sticks he injects 20 to 30 c.c. of Dakin's solution. The aspiration is repeated when there is marked pain or swelling. Daily injections of emetine—0.06 Gm.—are continued up to 6 to 10 doses. The aspiration method is advantageous in never requiring general anesthesia and in avoiding shock, the annoyance of dressings, and the pain of inserting tubes or packing; there is less chance of secondary infection, and his 10 cases, all of whom recovered, averaged but 11 days in the hospital. If aspiration fails, the patient is in a better condition for open operation. A. I. Ludlow (China Med. Jour., Feb., 1924).

Damp tropical climates, with the greater tendency to infection, exclude the open operation in all but very small abscesses, which are just the ones most difficult to reach except in the few with bulging in the epigastric region. Combination of the writer's statistics with those of Chatterji gives 264 cases treated by **aspiration, emetine and irrigation** of the cavity through the aspirating cannula, with a mortality of 6.4 per cent., as compared to 56.8 per cent. in 2661 cases treated by open operation in India and Mesopotamia up to 1921. To prove the value of sterile drainage of liver abscess, the author devised a flexible-sheath cannula for aspiration to be left in position in the abscess and connected by a long tube with a bottle of antiseptic under the bed. In a case thus treated, the discharge became reduced in a few days to a little clear serum, and the amebæ disappeared under ipecac. Sir Leonard Rogers (Proc. Internat. Conf. on Health Probl. in Trop. Amer., 1924).

Case of amebic dysentery with liver abscess and fatal ending, fairly typical in clinical history and course, unrecog-

nized until necropsy, and apparently contracted in New York. MacNeal and Klemperer (Amer. Jour. of Trop. Med., Sept., 1925).

TUMORS OF THE LIVER.

Of these, *secondary carcinomata* are, by far, the most common. *Primary carcinoma, sarcoma, angioma*, and *lymphadenoma* also occur. *Myxoma, cystosarcoma*, and *fibroma* are rare forms. Cancer of the liver is met with in about 3 per cent. of deaths from all causes, and in all persons affected with cancer the liver is the seat in 50 per cent. of the cases, the liver being third in order of frequency of internal cancer.

CARCINOMA.

SYMPTOMS.—In many, perhaps half, of the cases of cancer of the liver there are no symptoms by which the disease can be recognized during life. The symptoms of the primary growth usually overshadow those caused by the liver disease. The stomach is the seat of the primary growth in more than a quarter of all cases, so that symptoms of digestive disturbance are usually prominent, such as loss of appetite, distress after food, nausea, and vomiting. Progressive loss of flesh and strength is an early symptom. Pain and uneasiness in the hepatic region are common, but in many cases of even extensive disease of the liver neither is present. No doubt both are often due to local peritonitis.

Case of primary carcinoma of the liver with metastases in the lungs, in which thoracic pain, dyspnea, and hemoptysis dominated the clinical picture throughout, and a marked reduction in vital capacity afforded the first real evidence of the extent of progress of the intrathoracic morbid process. R. M. McKean (Amer. Jour. Med. Sci., May, 1922).

In a case of cirrhosis of 15 years' duration, there was found at autopsy an extensive transformation into both sarcoma and carcinoma, which had clearly developed, as shown by histological study, from the cirrhotic areas. The carcinoma started from regenerated tissue, and was stimulated by the sarcomatous process. R. H. Jaffé (Arch. of Int. Med., Mar., 1924).

The liver is usually enlarged. Hepatic dullness may extend upward to the fifth rib in the midaxillary line, to the left as far as the spleen, and the lower edge may be felt at or below the umbilicus. The lower edge and anterior surface below the costal margin are hard and often uneven on account of the nodular deposits. The nodules in some cases are felt to be umbilicated: an absolutely diagnostic sign. In cases of diffuse infiltration the liver may be very large; occasional instances are met with in which it is smaller than normal. The surface is smooth and hard and usually tender.

Jaundice is present in about half the cases. It is usually slight at first, becoming deeper toward the end. It is usually due to pressure on the common bile-duct in the transverse fissure by carcinomatous glands; it may be due to pressure on the branches in the liver by growing nodules, or, if the primary growth is in the head of the pancreas, it may press on the common bile-duct. It is important to remember that cancer of the liver is the most frequent cause of long-standing jaundice; it is permanent, and in the later stages may become extremely deep.

Ascites occurs in some cases, and is caused by pressure on the portal vein or extension of the cancer to the peritoneum. It is present in the cirrhotic form of cancer.

The superficial veins are enlarged. Some fever is not rare, continued or intermittent, especially when the disease runs a rapid course. It may occur in simple cancer, or may indicate suppuration. Hemorrhages into the skin or from the mucous surfaces may occur late in the disease.

Cancer of the liver tends to cause complications of various kinds which hasten the fatal outcome. Besides infections in the parotid glands, lungs, pleura, and peritoneum, there is a special tendency to local hemorrhage. Ascites may develop early with cancer of the liver and hemorrhage. This combination occurs with adenocancers and with liver tumors with cancerous invasion of the portal vein or its simple obstruction. Early death with cancer of the liver may be due to a subacute jaundice from hepatitis with secondary, galloping, local malignant disease. Or it may be the result of autogenic intoxication, acidosis, and acetonemia. M. Loeper (*Arch. des mal. de l'app. digestif*, Sept., 1911).

Death usually results within a few months; it is rarely delayed beyond a year after the symptoms have declared themselves. Occasionally the progress is delayed for some weeks at a time, during which some improvement may take place in the general condition. Death is usually due to progressive debility, with, in the last stage, some infection that closes the scene.

DIAGNOSIS.—The occurrence of progressive loss of flesh and strength, of pain and tenderness in the hepatic region, and of rapid enlargement of the liver, with the formation of nodules, forms a fairly sure basis for diagnosis. Even with this symptom group, difficulties may beset us. Hanot states that some cases of hepatic cancer closely resemble the

terminal stages of heart disease. But in the latter, slighter diminution of urea and albuminuria present, whereas absent in cancer, are the main differential points.

In the differential diagnosis between malignant and echinococcus disease of the liver, the age, over 50, speaks in favor of cancer; also a sudden onset of intense pain, enlargement of the liver, hard nodes on palpation, absence of eosinophilia and of leucocytosis in general, reduction of nitrogen and increase in urobilin in the urine, and coexistence of stomach trouble. The growth is more apt to be a sarcoma than a carcinoma if there are no extra-abdominal metastases, ascites, or jaundice. Ferranini (*Riforma medica*, xxxii, No. 44, 1916).

Apparent enlargement of the liver may be due to hardened feces in the transverse colon, which is tender, owing to the enteritis caused by the hard masses. Indurated puckered omentum and tumors of the stomach, kidney, and the abdominal wall may also simulate a large liver. The large cirrhotic liver may, in the early stage, be mistaken for cancer, as the liver is large and the jaundice usually well marked; but the liver is smooth and not tender and there is absence of the cachexia of cancer. The spleen is also large.

Syphilitic disease in which there is large amyloid liver with gummatous nodules may present some difficulties, as may also echinococcal liver with large cysts. In both, the history is more prolonged and there is absence of cachexia and usually of jaundice. Ascites is strongly indicative of cancer. The early period of cancer with cirrhosis may be indistinguishable from atrophic cirrhosis; there is similar jaundice and

ascites in both, but later the cachexia is more marked in cancer.

From hepatic abscess cancer is distinguished by the frequent history of a primary growth elsewhere or of hepatic irritation; the age of the patient; the relative absence of fever; cachexia; the more constant, dull and boring pain; the nodular tumor sometimes palpable, and the liver enlargement downward instead of upward.

Melanosarcoma usually involves other organs as well. It may cause great enlargement of the liver. Secondary tumors may form in the skin. In many cases there is melanuria—a characteristic symptom. Great difficulty is often experienced in differentiating cancer of neighboring organs from cancer of the liver, especially if they are adherent to the liver. Attempts have been made to apply functional hepatic tests to the early diagnosis of cancer of this organ.

In hepatic cancer with jaundice, the phenoltetrachlorophthalein test and the determination of the serum bilirubin furnish a sensitive and quantitative means of studying the effects of the jaundice. Of greater value, however, are the functional tests, especially the phenoltetrachlorophthalein test, in the cases without jaundice. In cases with clinical evidence of hepatic malignant disease confirmatory results were obtained by functional studies. In the absence of clinical evidence, the test alluded to may furnish the only evidence of metastatic nodules in the liver. Since the liver has a large margin of safety, positive tests, when obtained, become doubly significant. Greene, McVicar, Walters and Rowntree (*Arch. of Int. Med.*, Oct., 1925).

The chief interest in tongue-like accessory lobes of the liver is in connection with the diagnosis of abdominal tumors. Unless fully alive to the great variety, as to shape and

position, in which the accessory lobes of the liver may present themselves, one will often be misled.

ETIOLOGY.—Cancer of the liver is most frequently secondary to cancerous disease in the organs connected with the portal circulation. Hence it occurs secondarily to cancer of the stomach, rectum, colon, esophagus, gall-bladder, bile-ducts, and pancreas. It also follows cancer of the uterus, ovaries, and breast.

It occurs usually in late adult life, especially between the fortieth and sixtieth years, but may occur in children. The relative frequency of its occurrence in the sexes is doubtful; some observers state that it is more frequent in males, others in females. My own experience coincides with the former. Injury is a doubtful cause, and cancer of the bile-ducts is frequently associated with gall-stones.

MORBID ANATOMY.—As the primary growth is situated in some organ whose blood is carried to the liver by the portal vein, the liver becomes early affected, and often is the seat of large deposits at the time of death. The deposits are in the forms of whitish nodules scattered irregularly throughout the liver, just as we would expect, in view of infection through the blood of the portal vein. The nodules vary in size from a microscopical point up to a mass occupying a large portion of the organ. As they grow in the direction of least resistance they appear early beneath the capsule, and if the abdominal wall is thin they may be felt and even seen through it. They may be firm from fibrosis or soft from degeneration; the former shows umbilication on the surface, owing to contraction of the fibrous tissue. The

masses are globular, but coalescence may result in the formation of large irregular masses presenting, on section, a striking contrast to the liver tissue. Their color may be bright yellow, from bile staining; dark red, due to hemorrhage; or pale yellow, from fatty degeneration.

The secondary cancers are of the same structure as the primary one from which the infection was derived—usually alveolar or cylindrical carcinoma. The peritoneum over them may be thickened and strong adhesions formed with the abdominal wall or diaphragm. Usually some of the bile-ducts are compressed, obstructing the flow of bile.

Primary Cancer of the Liver.—Of this there are three forms:—

(a) A single large tumor with well-defined boundaries. It is usually grayish white, but may be the seat of hemorrhage.

(b) *Nodular growths* are the most common, and the whole liver resembles the appearance it presents when it is the seat of secondary carcinoma.

(c) *Cancer with Cirrhosis.*—This is a remarkably rare form. In it the cancer cells are uniformly diffused through the liver, so that the fibrous tissue is increased in all directions. This may contract and cause the liver, which at first is enlarged, to become smaller than normal. The organ looks like a coarse cirrhosis. When cut there are wide white bands seen running through the organ, the gland-tissue between them having vanished. Secondary growths in other parts of the body scarcely ever occur. Out of 258 cases recorded in the Berlin Pathological Institute in ten years, only 6 cases were true pri-

mary cancer of the liver, and of these 2 are doubtful.

Sarcoma.—Two forms of sarcoma occur, primary and secondary. The primary cannot be distinguished at the bedside from carcinoma, and even after death it is often difficult to differentiate them. The disease is extremely rare.

Secondary sarcomas of the liver exactly reproduce the form of the original growth. The patient usually dies before any symptoms are produced by them. Melanosarcoma is the most important form; it develops in the liver secondarily to sarcoma of the eye or of the skin. It is very rarely primary. The liver is greatly enlarged, and is affected by uniform infiltration or by nodular black masses. In the former case the cut surface is studded with black or brown granules.

There are usually metastases, affecting in some cases every organ in the body. Nodules of melanosarcoma in the skin may guide to the diagnosis (Osler).

Angioma.—Cavernous angiomas are common, but produce no symptoms during life. They occur as small, reddish bodies, and consist of dilated blood-vessels. They have, in children, occasionally produced large tumors.

TREATMENT.—As cancer of the liver is invariably fatal, nothing can be done unless it be through surgery.

Analysis of 76 cases of resection of the liver for hepatic neoplasms. The termination in the case of 2 patients was uncertain; of the remaining 74, 63 recovered, the operative mortality thus being 14.9 per cent. Shock, hemorrhage, and exhaustion caused death in 8 instances; septicemia in 2, and pulmonary embolism in 1. Four-

fifths of the patients were females, this proportion being attributed to tight lacing. Echinococcic and hydatid cysts were found in 20 instances; carcinoma in 17; syphiloma in 2; adenoma in 7; sarcoma in 5, and rarer forms of new growth in single instances. An early exploratory celiotomy advocated in every case. Keen (*Annals of Surgery*, Sept., 1899).

Portions of liver tissue of considerable size may be safely removed by previously rendering anemic the part which it is intended to remove. For the support of the ligatures, living tissue from the same animal, preferably the fascia and peritoneum from the abdominal wall, is best suited. The intraperitoneal or the intraparietal method is preferable to the external method. Carl Beck (*Jour. Amer. Med. Assoc.*, April 26, 1902).

New method of exposing the liver through the posterior surface of the right lobe. The patient, which the writer reports, was believed to have a tuberculous right kidney. There was pain on pressure in the lumbar region, which was believed to be due to the kidney. The latter was exposed from behind after resecting the twelfth rib and then pushed to one side after being freed from its attachments. The posterior aspect of the right lobe of the liver was thus exposed and on it was seen a tumor, which was removed. It proved to be a gumma and the patient made a good recovery under appropriate treatment. Although there may have been some doubt as to the propriety of surgical intervention in this case, still the advantage of reaching this region of the liver was shown. It is indispensable, however, that the pedicle of the kidney is sufficiently long to permit pushing the kidney to one side. J. Israel (*Deut. med. Woch.*, Mar. 31, 1904).

Case of pedunculated primary parenchymatous adenocarcinoma of the liver in an infant 10½ months old. It

is the first case reported in which complete surgical excision was done. There was a good surgical convalescence, with death sixteen days after operation from symptoms of acute enteritis. Castle (*Surg., Gynec., and Obstet.*, Apr., 1914).

The palliative treatment consists of an easily digested diet; carbonated waters, cracked ice and small doses of ipecac for nausea and vomiting; morphine for pain, and the ice-bag with chloral hydrate and bromides by rectum where marked delirium develops.

HYDATID CYST OF THE LIVER.

SYMPTOMS.—Small cysts cause no symptoms; they may be discovered at the autopsy. Cysts may reach considerable size without causing inconvenience and be discovered as a tumor-like enlargement accidentally. Quénu has, however, emphasized the existence of pain as a common symptom even in the earlier stages.

The liver enlarges irregularly and in time the cyst causes disturbance by pressing on some neighboring organ or part, interfering with its function. If in the dome of the liver it may displace the heart or lungs. It may press on the bile-passages, jaundice resulting; or on the portal vein, causing ascites. If it presses on the vena cava it causes edema of the legs. If superficial, the cyst may fluctuate on palpation, or, if tense, it may be felt as a hard solid mass. *Hydatid thrill* is sometimes obtained by placing one hand lightly on the cyst and tapping it gently with the fingers of the other hand. The thrill has been ascribed to the sudden impact of the daughter-cysts against each other and against the wall of the cyst; but thrill is sometimes ob-

tained in cysts which contain only clear fluid.

Rupture of the cyst may occur. If it takes place into any of the serous cavities, inflammation results. The pleura suffers most frequently; perforation of the lung often follows, with pneumonia and the expectoration of cysts and hooklets. More often pus, blood, and bile pigment are coughed up, such as occur in gangrene or abscess of the lung secondary to liver abscess.

The cyst may rupture into the stomach, as proved by the vomiting of cysts and hooklets; or into the intestine, with the appearance of these bodies in the feces, as would occur also if rupture takes place into the bile passages. Rupture may occur into the pelvis of the right kidney, followed by the presence of the hooklets and cysts in the urine.

Gaseous hydatid cysts of the liver may result from rupture into the bronchi or gastrointestinal tract, but sometimes the gas collection is primary. In a young girl who had had paroxysmal epigastric pains for several years, a more acute condition then developed with a tympanitic tumor above the lower border of the liver; this proved to be a hydatid cyst containing gas and pus, from which pure cultures of *B. proteus vulgaris* were obtained. The condition was treated by marsupialization, rapid recovery following. Such cysts generally remain latent until they become infected. Acute symptoms may then develop, or the patient may complain simply of anorexia, weakness and attacks of pain. The general symptoms point to an abdominal infection, the nature of which is shown by the tense, elastic swelling above the lower border of the liver, with tympany partly replaced by dullness when the patient sits up or leans forward. Succussion is another useful sign. Fluoroscopy might help, but is

seldom availed of on account of the acute condition present. The prognosis is grave, as cure is obtainable only by marsupialization. N. Fiesinger (Paris méd., May 17, 1924).

Apart from such accidents, the symptoms may consist only of trifling discomfort in the hepatic region.

Rupture of the cyst is often followed by severe urticaria; it has been attributed to a toxic material in the fluid. It may also follow aspiration of the cyst.

Sixteen cases of cyst perforation into the biliary passages. The literature shows, among biliary perforations, 23.8 per cent. into the common duct, 33.3 per cent. into the gall-bladder and cystic duct, and 42.9 per cent. into the hepatic duct. In liver colic with symptoms of common duct obstruction, accompanied by urticaria, such perforation of a hydatid cyst is probable. The mortality in operated cases was from 33 to 45 per cent. Prat and Piqueréz (An. de la Fac. de Med. de Montevideo, Mar., 1925).

In New South Wales, according to MacLaurin, epidemics of the disease have occurred 5 or 6 years after a year of exceptional rainfall. The abundance of vegetables in wet seasons results in a liability to infection from eating raw vegetables or preparing them for table during the wet season, while it is supposed to take 5 or 6 years for the disease to manifest itself after ingestion of the ova. Children are rarely affected, the greatest mortality occurring in middle life.

DIAGNOSIS.—This is not often made before the cyst has attained considerable dimensions; then the irregular enlargement of the liver for a long period, with the preservation of health, indicate hydatid disease. Upon aspiration of the cyst, if hooklets are found in the fluid, the diagnosis is confirmed, but such aspiration is held to be unwise owing to the risk of inducing suppuration by bringing bile laden with

colon bacilli into the cyst, as well as that of introducing infective material into the peritoneal cavity. A fluctuating tumor in the epigastrium is suggestive; it may give fremitus. Abscess of the liver is differentiated by the absence of symptoms of suppuration. It is difficult to distinguish a suppurating hydatid cyst unless the hooklets be found in the fluid. Cancer has been closely simulated by suppurating cyst. The clinical history usually serves to differentiate it. Dilated gall-bladder and hydronephrosis have been mistaken for hydatid cyst. A more common error is the mistaking of a cyst of the dome of the liver for right pleural effusion. Subdiaphragmatic abscess and purulent pleurisy secondary to rupture of a cyst are conditions difficult to distinguish unless the hooklets are found in the fluid.

Eichhorst believed of value, in the diagnosis of impending or actual perforation of the cyst, a characteristic aromatic odor, resembling that of boiled plums.

The X-ray, to which hydatid cysts are somewhat opaque, may give valuable diagnostic information.

Laboratory methods are likewise of great assistance. Eosinophilia is significant, though not constant. The complement fixation test, introduced by Weinberg, of Paris, has proven, with few exceptions, reliable. The Casoni intradermal test—analogueous to the Von Pirquet tuberculin test—is serviceable and often gives a positive reaction where other tests have failed. A specific precipitin test also gives satisfactory results.

Stress laid on the reduction of mortality, due to earlier treatment, obtainable with the laboratory diagnostic methods now available. The author found the *complement fixation test* absolutely specific; it proved negative in 917

cases free of clinical evidence of the disease. The most readily available and effective antigen consists of hydatid fluid containing scolices collected under sterile conditions from the liver or lung cysts of sheep. Fairley (Quart. Jour. of Med., Apr., 1922).

Even very small cysts can be diagnosed with the *intradermal skin test*, which consists in injecting 0.1 to 0.2 c.c. of hydatid vesicle contents of human origin into the skin of the forearm with a fine needle. Next day, in positive tests, there is a reddening and swelling over an area of the size of the palm, with marked inflammatory subcutaneous edema. Botteri (Wien. klin. Woch., May 25, 1922).

Blood examination and the precipitin and Casoni tests are within the reach of every practitioner and will yield a correct diagnosis in 80 to 90 per cent. of the cases. For the *precipitin test*, which gives results practically identical with those of complement fixation, the writer aspirates clear fluid from cysts in the liver and lungs of sheep, adds 1:10 of 5 per cent. phenol solution and mixes. On ice this antigen keeps for a week or longer. In making the test, equal parts of the antigen and the patient's serum are mixed and allowed to stand for 30 to 36 hours at room temperature before the final reading is made. In 23 proved and 2 probable hydatid cases the test was uniformly positive. Fairley (Med. Jour. of Austral., July 14, 1923).

The term hydatid is applied to the bladder worms, which are the larval forms of the *Tania echinococcus*: the minute tape-worm of the dog family. When fully grown the parasite is not more than 4 mm., or $\frac{1}{4}$ inch, long. It consists of 4 segments, of which the last alone has fully formed sexual organs. It is very common in dogs of Iceland and Victoria (Australia); also in the Icelandic settlements in Manitoba (Canada), the dogs having been brought from Iceland. The

ova of the echinococcus are expelled with the excrement and find their way into the alimentary canal of man by water and green vegetables; also by direct contact with infested dogs, to the hair of which ova adhere and may be carried to the mouths of those who touch the dogs. The disease is rare in Canada and the United States, as well as in European countries, because the dogs are rarely infested, else hydatids would be frequent among all classes, irrespective of habits as to cleanliness.

MORBID ANATOMY.—The ovum, having entered the human stomach, loses its covering by digestion, setting free the larva, which, by its hooklets, burrows through the intestinal wall. Some of them meet with and enter a branch of the portal vein and are carried to the liver, where they lose their hooklets, and their cystic development begins. The cyst contains a clear non-albuminous fluid inclosed in a capsule of two layers. There is an outer, thick, homogeneous, laminated, elastic membrane which coils upon itself wherever cut and if withdrawn displays a tremulous motion. This is the *ectocyst* of Huxley. Within and closely in contact to this lies the *endocyst*: a delicate, thin, soft, granulated membrane, forming the vital part of the bladder worm. Outside the capsule there is usually a thick investment derived from the tissues of the infested organ. After the cyst has attained considerable size buds are produced from the inner membrane, which gradually develop into cysts having the two walls identical with the parent cyst. From these daughter cysts similar buds develop and form a tertiary series—the granddaughter

cysts,—and so on indefinitely. In time each of these cysts severs its attachment to the parent and becomes independent. From the inner membrane or endocyst of all these cysts buds arise and become transformed into scolices, or echinococcal heads, presenting a circle of hooklets along with sucking disks. Each of these, transferred to the intestine of a dog, may develop into a tape-worm. The exact manner of the development of these buds is in dispute. It is thus apparent that there is a striking contrast between the development of this parasite and of the *Tania solium*. The ovum of the latter develops into only one larva capable of producing only one tape-worm, while the ovum of the *Tania echinococcus* produces a larva capable of multiplying itself indefinitely, so that from it an innumerable number of tape-worms may result.

The hydatid cyst is usually single, the daughter cysts being within the cavity of the mother cyst, which may be of enormous size, filling the abdomen and pushing the diaphragm high into the thorax. The liver tissue is atrophied in proportion to the size of the cyst; that is, the pressure to which it is subjected. The parasite may die. Then the fluid becomes absorbed, the capsule shrivels, and within its remains are found fat drops, cholesterin crystals, and hooklets. The capsule may become inflamed and an abscess result.

In lower animals the cyst may be multiple, the daughter cysts developing outward from the mother cyst: exogenous development.

A third form is multilocular. In this the daughter cysts are surrounded by fibrous tissue and all become con-

solidated into a multilocular mass resembling a colloid cancer, for which it was formerly mistaken.

PROGNOSIS.—Hydatid cyst of the liver is a serious disease, proving fatal in 13 to 25 per cent. of the cases. The course of the disease is chronic, sometimes lasting as long as thirty years. Recovery may follow death of the echinococcus, which occurs occasionally, possibly from escape of bile or blood into the cyst. As a rule, the cyst ruptures on account of its continued increase in size. The rupture may take place into the peritoneal cavity and this may be fatal from shock; the fluid, being sterile, does not cause septic peritonitis, but the subject may succumb a few months later to cachexia from secondary echinococcosis.

If inflammatory adhesions to the stomach, small intestine, colon, or right kidney have preceded the rupture, the cyst may rupture into one of these organs, with discharge of the fluid by vomiting, diarrhea, or with the urine. If the cyst is situated in the dome of the liver it may rupture into the pleura or pericardium. The latter is fatal, but recovery may follow discharge through a bronchus. Rupture may occur into the hepatic vein, or the vena cava, and cause sudden death. The cyst may open into the bile passages and recovery follow, although grave symptoms usually result from obstruction and infection.

The most favorable result is by adhesion to the abdominal wall and perforation externally, usually near the umbilicus. The cyst frequently suppurates, pyogenic organisms gaining access to the cavity by the blood or bile, or from a neighboring inflammatory focus.

TREATMENT.—**Operation** alone offers hope of relief, and brilliant results have followed such intervention. The simplest operation consists in **aspiration**, and is sometimes successful. If not, **injection of antiseptic fluid** should be resorted to. Various antiseptics have been recommended, the best of which is probably **formaldehyde solution**, 1 to 10 per cent. **Silver nitrate solution**, 1 : 500, has also been recommended; it is said to act by precipitating the chlorides and leading to the death of the parasite. These procedures entail some risk of secondary infestation of the peritoneum, infection of the cyst, or mild intoxication of an anaphylactic type (Dévé).

The most approved procedure is **operative incision and drainage**. In the procedure known as **marsupialization**, after incision over the cyst the peritoneal cavity is walled off, the edges of the incision protected with gauze, as much as possible of the fluid evacuated with an aspirating trocar, the cavity explored and further emptied with the fingers, gauze packing inserted, and the incision in the liver sutured to the peritoneum. The cavity is repacked at intervals until the cyst contracts and finally closes. Instead, **enucleation** of the cyst is sometimes carried out, both the liver cavity and the external wound being then, if possible, completely sutured, or if not, drained with rubber tissue.

Seventy cases treated by simple **marsupialization**, together with the insertion of a **drainage-tube** into the cyst cavity for several days to maintain a sinus and insure healing from the bottom. There were but 7 deaths, although 19 of the cysts were suppurating. Two of the deaths were in suppurating cases, 3 deaths in cases with ruptured cysts and general peritonitis,

and the others in complicated cases. The average time for healing is 3 to 6 weeks. C. MacLaurin (Brit. Med. Jour., Jan. 10, 1914).

The ideal procedure is, after emptying the cyst as well as possible, to leave 10 per cent. formaldehyde solution in it to destroy any residual hydatid elements. The writer leaves as much as 45 c.c. (1½ ounces) in the sac. The adventitia and abdominal incision are then sutured completely. Kilvington (Med. Jour. of Austral., Dec. 17, 1921).

Case in which intramuscular injections of colloidal antimony and emetine seemed curative. Cawston (Jour. of Trop. Med. and Hyg., Feb. 1, 1922).

In operating for hydatid cyst the author generally uses local anesthesia. The cyst wall is sutured into the skin wound, then opened and the fluid allowed to run out spontaneously; what remains is evacuated by change of posture or, if this is not practicable, by siphon drainage. The membrane is then drawn out with forceps wrapped with gauze. In infected cysts the membrane is not removed. Irrigations are used in the after-treatment only if there is fever for several days. In non-infected cysts the operative mortality is very low. Multiple cysts entail far more risk, and when in the abdomen seem thus far to be incurable. The writer's general mortality has been 5 per cent. Lozano (Münch. med. Woch., July 27, 1923).

Primary suture of the echinococcic sac after killing of the parasites with formaldehyde solution and evacuation is preferable to drainage of the cyst, notwithstanding possible complications, and should be carried out in the uninfected cases. Fixation of the sutured part of the liver near the abdominal incision is indispensable with this method. F. Partsch (Deut. Zeit. f. Chir., Mar., 1924).

Electrolysis and potassium iodide have been successful in a few cases.

Non-parasitic Cysts.

This form of cyst, according to Boyd, occurs mainly in females and

has been met with in infancy as well as in old age. The signs are abdominal swelling with fluctuation but of low tension, a characteristic of these cases. They progress rapidly if neglected, while the prognosis is not unfavorable if surgical treatment is promptly resorted to.

Treatment.—Surgical removal is indicated as soon as the condition is recognized. Simple puncture should be avoided, since it has often proved fatal.

Miscellaneous Parasites.—The liver may contain the *Pentastomum denticulatum*, the larval form of *Linguatula tanioides*, the adult worm of which is lancet-shaped, marked with numerous rings and commonly found in the nostrils. The *Coccidium oviforme* is common in the liver of the rabbit, forming whitish nodules and producing phenomena resembling those caused by malaria, besides tenderness over the liver, diarrhea, and nausea.

AMYLOID LIVER (Lardaceous Liver; Waxy Liver).—This condition is characterized by an infiltration of the liver by a so-called amyloid substance, which has been shown to be, in reality, related to coagulated proteins.

SYMPTOMS.—There are no characteristic symptoms of amyloid liver. The patient presents the symptoms of the primary disease. He is pale, cachectic, and later may be dropsical. There is no jaundice nor bile pigment in the urine. Bile is secreted and flows into the intestines, coloring the contents. There are disturbance of digestion and often diarrhea, on account of the amyloid deposit in the intestine. The urine is usually copious, pale, of low specific gravity,

and contains much albumin on account of the amyloid disease of the kidneys.

On physical examination the liver is found large, firm, smooth, and not tender. Its lower edge is usually rounded, but sometimes sharp, and not rarely as low as the iliac crest. There are no signs of portal obstruction. The spleen may be large, on account, chiefly, of the amyloid change in it.

The general condition grows gradually worse, the skin assumes an earthy pallor, which, some believe, is characteristic, and the patient dies from exhaustion, if not cut off by an intercurrent affection or a "terminal infection."

The duration of the disease is usually several years, although occasional cases run their course in a few months.

DIAGNOSIS.—This is usually easy from the associated conditions. The occurrence of progressive enlargement of the liver in a case of long-standing suppuration, especially of a tuberculous or syphilitic character, renders the diagnosis almost certain. The coexistence of degeneration of the kidneys, spleen, and intestines adds to the certainty of the diagnosis.

ETIOLOGY.—In amyloid liver a deposit of waxy material takes place in the blood-vessels and interstitial tissue of the liver. It occurs as part of a general degeneration in certain constitutional conditions, of which prolonged tuberculous suppurations of the bones, lungs, and urinary tract are the most frequent. Next to these, syphilitic suppurations are the most common causes; but the amyloid change may occur in syphilis without suppuration. It is also occa-

sionally found in rickets, Bright's disease, leukemia, malignant disease, and in protracted convalescence from infectious fevers.

MORBID ANATOMY.—In advanced stages the liver is greatly and uniformly enlarged. Its size may be doubled and its weight more than trebled. The surface is smooth, firm, and of a slightly glistening yellowish gray color. On section the surface has an anemic, waxy appearance, is semitranslucent in thin sections, and the infiltrated areas stain a rich mahogany-brown on the application of a dilute solution of iodine, while the normal parts become a light yellow.

The morbid change usually affects the capillaries in the middle zone of the hepatic lobules first, and later the interlobular vessels and connective tissue. In the capillaries "the amyloid substance lies between the endothelium and the liver cells, and the latter atrophy apparently because of the pressure which the amyloid substance exerts. Some of the cells show fatty and albuminous degeneration" (Thoma).

Similar changes are usually found in the spleen, kidneys, and mucous membranes of the intestines.

Amyloid disease of the liver is localized to the tiny blood-vessels at first, to the walls of the trabecular capillaries; later, of the intralobular capillaries. Amyloid matter forms a solid cylinder of the former arterial walls, with almost total obliteration of the lumen of the vessel. When the liver cells show changes, these begin near the affected capillaries. Thus it is that specimens may show three layers in a lobule—a narrow periphery of fatty degeneration, normal liver cells in the center, and between them the intermediate layer

showing the changes of amyloid degeneration. The cell granulations are gradually replaced by this material. Others claim that the hepatic cells never become amyloid, the changes found in them being due to mechanical forces alone. The author gives a detailed description of the histological findings in 2 cases of amyloid disease of the liver. His investigations show that amyloid degeneration is not seen in the liver cells at all, the changes there found being those of compression, deformity, and atrophy, always secondary and mechanical. B. Auché (Jour. de méd. de Bordeaux, Sept. 15, 1901).

PROGNOSIS.—The prognosis is bad. Many, however, claim that a cure is possible in the initial stage if the cause is removed.

TREATMENT.—There is no effective remedy for the disease known; therefore the treatment should be prophylactic, *i.e.*, removal of the cause.

Tuberculous disease of bones should be treated surgically and cured as soon as possible, as should also chronic suppurations of all kinds. Syphilis should be vigorously treated. The patient should be nourished and the strength maintained as well as possible.

SYPHILIS OF THE LIVER.

Various morbid conditions may be caused by the specific agent of syphilis. Hepatic syphilis may be *inherited*, the organ becoming first enlarged and hardened, then reduced in size and lobular owing to the formation of connective tissue, or, rarely in inherited syphilis, be the seat of gumma. Or, it may be the result of *acquired* syphilis, as a tertiary manifestation, either in the form of interstitial hepatitis, gumma, amyloid disease or, rarely *endarteritis*.

Cases of syphiloma on the surface of the organ are, according to certain writers, rare. This does not accord with the writer's personal experience. With one or two exceptions, the tumor has been attached to the left lobe of the liver. This is a point which should ever be borne in mind. J. M. Anders (Jour. Amer. Med. Assoc., June 22, 1912).

The gumma is the lesion most frequently observed. It may range in size from that of a pea to that of an orange, its favorite seat being the convexity of the organ close to the suspensory ligament, though at times found in the organ or the connective tissue of the vessels. Central cheesy degeneration and fibrosis then follow in turn with increasing impairment of function.

SYMPTOMS.—Though infrequent, jaundice may occur owing to portal obstruction; it may be slight, moderate, or severe, but usually develops rapidly. Anorexia, nausea, bitter taste in the mouth, diarrhea, and pain in the epigastrium usually precede the icterus. Loss of weight is usual, and fever is commonly observed. As to the physical signs, general enlargement of the liver with nodules or large rounded masses are the most common, the left lobe being relatively much larger than the right as observed by McCrae. Ascites is sometimes observed.

The clinical statistics underestimate the frequency of syphilis of the liver. The Wassermann reaction will increase the number of cases. The symptom-complex of syphilis of the liver is not pathognomonic, as it simulates almost every hepatic disease; occasionally it simulates febrile diseases. Whenever the diagnosis is uncertain, resort should be had to the therapeutic test as well as to the Wassermann reaction. Frequently

mixed treatment has a striking effect on lues of the liver, regardless of the time it has existed. Schragar (Jour. Amer. Med. Assoc., Mar. 9, 1912).

Case which represents an important group of cases of hepatic syphilis, in which the disease resembles ordinary cirrhosis of the liver. The symptoms are usually those of pain in the right hypochondrium, with more or less gastric disturbance, occasional hematemesis, and ascites. Jaundice and ascites are rare. The liver and spleen are found to be enlarged and firm. Pain generally is a prominent symptom, owing to the perihepatitis and perisplenitis. The diagnosis rests on the preponderance of syphilis over alcohol in the history, and the relief of symptoms by antisyphilitic treatment. Core (Lancet, Mar. 8, 1913).

TREATMENT.—While this cannot influence the results of the syphilitic process, cirrhosis, amyloid, etc., the causative condition demands the prompt use of **arsphenamin**, **mercurial injections** or **inunctions**, **bismuth**, or **potassium iodide**. A very prompt favorable result may thus be frequently obtained.

The treatment is the usual therapy for syphilis, with special emphasis on **potassium iodide**. In many of the cases this alone was given with a perfect result. No difference could be observed when **mercury** was added, but it seems wise to give both drugs. Almost immediate disappearance of the fever, reduction in the size of the liver and nodules, and rapid gain in the general state and weight occur when iodide alone is given. **Arsphenamin** was given to 3 patients, in doses of 0.5 or 0.6 Gm. ($7\frac{1}{2}$ or 9 grains), and in 2 of these mercury and iodide were not given in order that the effect might be watched. Improvement followed in both cases, but not so rapidly as was the case with iodide alone or mercury and iodide. Thomas McCrae (Jour. Amer. Med. Assoc., June 22, 1912).

Acute pain and hepatic swelling are to be expected in tertiary syphilitic hepatitis. In 2 out of 4 cases referred to, an operation was performed; the third patient refused operation and the fourth was thought at first to have an inoperable stomach cancer. Two patients had irregular but persistent fever for several weeks; this was controlled in a few days by **antisyphilitic treatment**. One patient had bilateral pleural effusion, tapped 5 times. Pain was marked in all cases, and tumor was present in 3. Only 2 patients gave a history of syphilis. **Neosarsphenamin** was given at first and followed by injections of **mercury cyanide** or **bismuth**, with very good results in all cases. Denéchau, Fruchaud-Brin and Agoulon (Bull. Soc. méd. des hôp. de Paris, Apr. 26, 1923).

Case of caseated gumma of the liver, with laparotomy and **enucleation** of the mass. The patient had suffered several weeks from an indefinite tumefaction between the umbilicus and right costal arch. The tumor was found of fist size, close to the origin of the hepato-umbilical ligament, and surrounded by apparently normal liver tissue. Recovery took place without complications. In all doubtful tumors of the upper abdomen the Wassermann reaction should be carried out. A positive result does not, however, absolutely prove the syphilitic nature of the condition, and exploratory laparotomy is therefore indicated in any case. A relatively recent, well-circumscribed gumma may, under favorable conditions, be removed; otherwise, internal treatment alone is indicated. If adjoining organs are threatened or already involved by perigummatous contraction, or in tumors histologically doubtful, removal is in order. E. Monse (Beitr. z. klin. Chir., cxxviii, 148, 1923).

TUBERCULOSIS OF THE LIVER.

The liver may be involved in the course of miliary tuberculosis or secondarily to tuberculosis of the lungs or intestines. A few cases of

primary hepatic tuberculosis have been reported. Although the organs may be crowded with tubercles, jaundice is only occasionally observed. The organ may be enlarged and lobular. Emaciation progresses rapidly and the temperature is that of general tuberculosis. The disease is somewhat more frequent in children than in adults.

In 2 personal cases much the same train of symptoms occurred, although the first was much more acute. In each there was marked jaundice. The temperature and general condition were obviously those of tuberculosis. The liver was particularly involved. In the first case the liver and spleen seemed to be the only two organs affected. In the second the disease was more widespread and much less acute, but in this case also the most extensive disease was jaundice of the liver and spleen. Milne (N. Y. Med. Jour., May 10, 1913).

Analysis of 34 cases of "conglomerate tubercle" the writer has compiled from the literature, and 13 of a tuberculous abscess in or near the liver. In 30 of the cases the tuberculous process was a necropsy discovery. In 23 there had been no signs during life of any abdominal trouble. An operation was undertaken in 15 cases, but on an erroneous diagnosis in all but 3 instances. As long as the process is in an incipient stage or restricted to the inside of the liver, the symptoms are merely those of gastrointestinal disturbance. Not until the process reaches the surface of the liver or spreads beyond it does its true nature become manifest. It may then appear as a tumor or there may be evidences of irritation of the peritoneum with perihepatic abscesses. Lotheissen (Beiträge z. klin. Chir., lxxxix, H. 5, 1913).

TREATMENT.—The treatment is that of the tuberculous process, with **open air, potassium iodide, and creosote carbonate** as sheet anchors.

The writer emphasizes the necessity for general treatment for the tuberculosis, including exposure to **direct sunlight**. Complete recovery may be anticipated if treatment is commenced early enough and the patient has the resisting powers of youth, and the operation is managed in such a way as not to make too much demands on his strength. The tumor should be removed after intrahepatic ligation of vessels. Wendel has reported the excellent outcome a year later after **resection** of 940 Gm. of **liver tissue** for an adenomatous growth. The **cavity** left must be **tamponed**. **Resection of ribs** may be necessary, and the writer found it advisable to resect only two or three at a time, thus fractioning the operation; in 1 case he thus removed separately 3 cheesy foci, each nearly as large as a man's fist. Local anesthesia with primary ether **anesthesia** or the "twilight sleep" is ample for the **fractioned operation**. In 10 of the 15 operative cases the patients recovered although the tuberculous process was far advanced. The writer advises not to let the propitious hour for **operative treatment** slip past while trying antisyphilitic treatment. G. Lotheissen (Beiträge z. klin. Chir., Bd. lxxxix, H. 5, 1913).

FATTY LIVER.

Fatty liver occurs under two forms: *fatty infiltration* and *fatty degeneration*. The former represents a normal condition, since liver-cells always contain some minute globules of fat. In this form the particles of fat penetrate the liver cells, where they coalesce into growing droplets and push aside the cell protoplasm, and often destroy it by interfering with its nutrition.

In fatty degeneration there is a conversion of the protoplasm itself of the cell into fat, probably by the action of some toxic agents, such as phosphorus.

FATTY INFILTRATION.

SYMPTOMS.—There are no distinctive symptoms. The liver may, if large, be felt to be smooth, soft, not tender, and with rounded edges. There is no jaundice. Addison long ago drew attention to a semitransparent, pale, smooth, soft skin, feeling like softest satin, occurring in fatty liver. He considered it almost pathognomonic. And Hebra noticed a similar condition of skin in habitual spirit drinkers, and in them fatty liver is common.

DIAGNOSIS.—The fatty liver can usually be recognized by its soft, smooth character and its occurring in the obese or the emaciated. The large amyloid liver is distinguished by being firm, larger, and by the history of the cause and the evidence of renal disease.

ETIOLOGY.—The conditions under which fatty infiltration occurs may be divided into two main classes, strikingly in contrast with each other. In one class the fatty liver results from dietetic errors, from eating an oversupply of rich food, and as a part of general obesity, chiefly in persons of sedentary habits. The blood is overcharged with fat, of which much is stored in the hepatic cells.

The other class consists of cachectic cases, of which pulmonary phthisis furnishes the greater number. In these, on account of the low powers of oxidation, even the small amount of food that is taken is not properly oxidized and much of it is converted into fat and deposited in the liver cells.

MORBID ANATOMY.—The liver is large, smooth, and soft. It may weigh 10 or 12 pounds. The edge is

thick and rounded. The deposit of fat begins in the cells at the periphery of the lobule, and in time distends them. It can be extracted from the cell with ether, leaving the cell shrunk.

The specific gravity of the liver is reduced, so that the whole organ floats when placed in water.

PROGNOSIS.—This will depend on the cause. If the condition that leads to the deposit of fat in the liver is relieved the further deposit of fat will cease and the hepatic cells will gradually be restored to their normal condition.

TREATMENT.—Treatment should, therefore, be directed to **removal of the cause** of the condition. In the obese there should be a careful **regulation of diet**, with a view to lessening the formation of fat while sustaining the strength. Habits of **early rising** and active **exercise** should be encouraged, care being taken not to induce overfatigue, especially if the heart shows signs of weakness, as it often does from fatty infiltration or degeneration. **Water** should be **freely taken** on an empty stomach, and **occasional purging** resorted to. **Little**, if any, **alcoholic stimulants**, especially beer, should be **allowed**. If sufficient active exercise cannot be taken, **massage** and **resistance movements** will, to a great extent, supply its place.

In the anemic form of fatty liver, such as occurs in pulmonary phthisis, the treatment should aim at improving the general condition without regard to the liver.

FATTY DEGENERATION.

This results from poisoning of some form, as in acute yellow atrophy,

in which the liver changes are typical of fatty degeneration.

DISEASES OF THE GALL-BLADDER.

GALL-TRACT, NON-SURGICAL DRAINAGE OF.—This refers to a diagnostic and therapeutic procedure developed by B. B. V. Lyon, on the basis of a suggestion by Meltzer that the introduction of 25 per cent. magnesium sulphate into the duodenum through the duodenal tube might relax the sphincter of the common duct and permit the ejection of bile.

Clinical Procedure.—The patient presents himself after fasting 20 hours. He brushes his teeth carefully, rinses and gargles his mouth and throat thoroughly, first with **potassium permanganate** solution (gr. j-3j), then with a mildly astringent solution of **zinc chloride**. The duodenal tube, after standing over night in 2 per cent. **lysol** solution, is sterilized by boiling and passed to the stomach. The fasting residue is aspirated and set aside for chemical, cytologic and bacteriologic examination. The stomach is then rinsed to sparkling clearness by gravity douching from a 250 c.c. tank or syringe, the wash-water being recovered in 250 c.c. conical graduates. It is next made astringent with a zinc chloride solution and rewashed thoroughly, and is then disinfected with 250 c.c. of 1:10,000 potassium permanganate and again washed to crystal clearness. This requires about 20 minutes.

The **duodenal tube** is then connected to the first sterile aspirating bottle, and the duodenal secretion is aspirated, to note whether the common duct sphincter is normally closed. That the tube has entered the duodenum is known by a change from acid to alkaline reaction and a slight "tug" felt upon exerting gentle traction on the tube. The duodenum is then douched with about 75 c.c. of a 33 per cent. solution of **magnesium sulphate**.

Within 1 to 6 minutes, normally, after the start of the aspiration, the sphincter is relaxed and the returning magnesium sulphate becomes tinged with bile, which becomes steadily deeper until pure bile alone is being recovered. When the first or A bile—believed to come from the common duct, with a little from the cystic duct and liver—becomes a distinctly deeper golden-

yellow or in any way off color and of heavier viscosity, the bottle is detached and drainage allowed to continue until the third transition to a much lighter yellow and thinner bile appears, when a final bottle is attached.

The darker or B bile is asserted to come almost exclusively from the gall-bladder, while the light yellow limpid C bile, appearing normally at the third transition, is considered to be bile freshly secreted by the liver.

The final step in the routine method consists in introducing, for local healing purposes, 250 c.c. of **Ringer's solution** at 105° F., at least twenty minutes being consumed in the process. A copious bowel movement generally follows.

Nature of Findings.—The contents of the fasting stomach is measured, examined for consistency, mucus, acidities, bile, occult blood, and micro-organisms, and compared with the duodenal findings. The bile obtained from the duodenum after introduction of magnesium sulphate is examined for color, consistency, viscosity, transparency, mucus, cells, crystals, debris, concretions, lecithin, cholesterin, calcium, pigments, etc. A careful bacteriologic examination is also promptly carried out.

Lyon states that in *cholecystitis without choledochitis*, the first bile collected is relatively normal, but the second bile is grossly pathologic, being more viscid than normal gall-bladder bile and turbid, with flaky or stringy mucus. It contains pus cells, desquamated epithelium, and sometimes erythrocytes, and cultures show pathogenic organisms, such as streptococci of various strains, the typhoid or pyocyaneus germs, and the catarrhalis organism. The color varies from deep, golden yellow to a dark molasses yellow, a light mustard yellow, and various shades of green or greenish black.

In *cholelithiasis* there is the evidence of cholecystitis and also sometimes a gritty or sand-like sediment found microscopically to consist of crystals of bile salts; at times, small gall-stones have been noted.

In *choledochitis* the bile first collected is abnormal, being viscid, with an excess of flaky mucus, usually turbid and off color, and containing pus cells enmeshed in mucus, epithelial cells, and occasionally

erythrocytes. Cultures may show pathogenic germs.

Use in Diagnosis.—The procedure is offered as a means of diagnosis of biliary diseases supplementing the usual clinical methods, including the X-rays. Reporting on 100 consecutive gall-tract cases, Lyon, Bartle and Ellison (Amer. Jour. Med. Sci., Jan. 1922) stated that 68 of these would have failed of diagnosis by ordinary procedures. Of 93 cases with positive bacteriology, streptococci were isolated in 50 per cent., staphylococci in 25 per cent., *B. coli* in 15 per cent., *B. subtilis* in 8 per cent., *B. pyocyaneus* in 1 per cent. and *B. typhosus* in 1 per cent. The final diagnoses in the 100 cases, based on the non-surgical drainage as well as other findings, comprised: Gall-bladder syndromes, 27; gall-stone syndromes, 4; mixed syndrome (ulcer, appendix, gall-bladder), 22, and vague atonic dyspepsia (with or without biliousness), 47.

G. M. Piersol and Bockus (Amer. Jour. Med. Sci., Apr., 1923) deem bacteriologic study of bile obtained by the Lyon procedure feasible and important, and lay stress on replanting from the original broth culture, if one is used, in 6 hours; otherwise a rapidly growing colon bacillus may make it extremely difficult to isolate the slower growing streptococcus, if present. To be doubly safe, bile is planted on broth cultures during the biliary drainage and transplanted within 12 hours. Besides, all the bile withdrawn is collected in bottles, separated into "A," "B" and "C" fractions, and streak cultures made from these fractions on solid media at once. Cases are adduced to show the value of the therapeutic indications (vaccine therapy) afforded by such bacteriologic studies.

In the experience of M. L. Wilbanks (Tex. State Jour. of Med., Mar., 1924), when there is present inspissated mucus or tarry bile, recovery of bile may be impossible, especially during the first drainage attempted. In general, however, failure to obtain gall-bladder bile after stimulation with magnesium sulphate indicates complete obstruction of the cystic duct, due either to stones, adhesions or pressure from without by a tumor.

After a study of 274 cases, C. M. Jones (Arch. of Int. Med., July, 1924) emphasized high-speed centrifugalization of the duo-

denal contents as the only means of securing consistent sediment findings. Abnormal findings consisted of bile-stained epithelium or leukocytes, and cholesterol, bilirubin or calcium-bilirubin crystals. In cholelithiasis, characteristic sediments were found, consisting of abnormal amounts of any or all of the foregoing crystalline elements.

M. J. Synnott (Jour. Amer. Med. Assoc., Nov. 14, 1925), in following the Lyon technique, rarely washes out the stomach, having found that it hinders passage of the tube into the duodenum. After the tube has been swallowed to the 55 cm. mark he pours in 100 c.c. of water, and has the patient lie on his right side and swallow very slowly, taking 20 minutes to do so, to the 75 cm. mark. Every case of diabetes should be examined by the Lyon method, for in some cases ascending duct infections or gall-bladder infections extending into the pancreas play an important part in causing the disease and call for therapeutic drainages.

Use in Treatment.—The conditions in which the procedure has proven therapeutically useful are enumerated by Smithies and his associates as follows: (1) **Acute choledochitis, cholecystitis or hepatitis**, arising independently or in association with acute infectious ailments, such as pneumonia. (2) **Hepatitis** with faulty duct action from ptomain, lead or phosphorus poisoning, and acute yellow atrophy, as from arsenical injections. (3) **Biliary stasis** in connection with acute or chronic heart trouble, hepatic cirrhosis, or infection in anemias such as hemolytic pernicious anemia or Banti's syndrome, or stasis or infection during diabetes, pancreatitis, or exophthalmic goiter. (4) Attacks of **biliousness** in conjunction with migraine, epilepsy, etc. (5) **Rheumatoid infections** with biliary tract involvement, persisting after removal of foci of infection. (6) **Pyloric or duodenal ulcer** recurring with bilious attacks or atypical ulcer manifestations, when reliable surgical treatment is not available. (7) **Intestinal stasis** with biliary and hepatic types of dyspepsia, and attacks of mucous colitis. (8) After operation on the biliary organs, if deranged function continues and further surgery is not possible. (9) **Biliary infection** without gross mechanical defects, stones, or new formations.

According to G. M. Niles (Jour. Med.

Assoc. of Georgia, Apr., 1924), the procedure may either mitigate symptoms or prove curative in the following conditions:

(1) **Chronic cholecystitis or choledochitis**, as indicated by flatulence, dyspepsia, muddy skin, anorexia, constipation and malaria—a syndrome commonly known as biliousness. (2) **Biliary stasis** with chronic gall-bladder infection following malaria, typhoid, influenza or constipation. (3) **Sick headache**; in cases of long standing many drainages may be required. (4) Some forms of **asthma**, where the sensitization tests have not worked out satisfactorily, or where the cause is probably an infected gall-tract. (5) **Infectious joint troubles**, as an adjunct to other measures. (6) **Chronic catarrhal jaundice**, without a material obstruction, such as a large stone in the common duct. Cases operated for **gall-stones** or other conditions can be made much more comfortable by several drainages before and after operation. Amelioration is also afforded in various cases in which operative intervention is for some reason inexpedient.

To secure permanent improvement in the more severe grades of **hepatitis, cirrhosis, cholangitis and pancreatitis**, as well as in gall-tract disease associated with **duodenitis** or the medical form of **duodenal ulcer**, Lyon and Swalm (Jour. Amer. Med. Assoc., Nov. 14, 1925) advocate *continuous drainage*. In this procedure the tube is kept in for 24 or more hours at a time, and the patient fed through the tube. The prolonged drainage is repeated every 2 days for 2 to 4 weeks, until from 3 to 6 gallons of bile mixture has been recovered. This thoroughly drains the liver, flushes ducts, avoids secondary stasis, and likewise drains the pancreas.

INFLAMMATION OF THE BILE PASSAGES AND GALL-BLADDER (ANGIOCHOLITIS OR CHOLANGITIS AND CHOLECYSTITIS).—Definition. — This is an inflammation of the biliary tract due in most instances to infection by pathogenic bacteria. It may affect the common bile-duct and all its branches or any part of them, the cystic duct, or the gall-bladder, and may be acute and chronic.

Symptoms.—Since *acute catarrhal cholangitis* nearly always follows gastroenteric catarrh, the usual acute dyspeptic symptoms precede those due to the disease of the bile-ducts; such as anorexia, belching of gas, epigastric distension, nausea, vomiting, and constipation. These symptoms may, however, be very mild, or most of them may be absent, and jaundice be the first symptom noticed. The jaundice deepens rapidly, but is always of a bright-yellow tint, never the green or bronzed hue of that due to malignant disease.

The stools are clay-colored and the urine contains bile pigment. The temperature may be slightly elevated. The pulse is usually normal, but may be slow, being only 40 or 50 to the minute. A dull, heavy, sleepy condition may be present. The liver is sometimes enlarged and palpable below the costal margin.

Bile duct infection unaccompanied by visible disease of the duct walls or suppuration has been termed *cholangia* by Naunyn. This condition may be either hematogenous or enterogenous. In the former, the infection begins in the larger ducts and creeps up to the bile capillaries, giving rise to *cholangitis lenta*, in which anhemolytic streptococci may be found in the blood. In the other type, digestive disturbances are prominent. Jaundice is present in involvement of the finer ducts, but the stools may retain their color if a portion of the liver is uninvolved. Cholangia may be attended with colic in spite of the absence of stones. Chills often occur at the outset, but the temperature may not be high; in prolonged cases, there is usually remittent fever. Other features are enlargement and tenderness of the liver and splenomegaly, and in protracted cases ascites, Banti's disease being thus simulated. F. Ueber (Klin. Woch., Mar. 26, 1923).

If the catarrhal inflammation is confined to the gall-bladder (*cholecystitis*), the cystic duct usually becomes obstructed by pressure of the bladder contents on the outlet. No jaundice occurs, or any of the foregoing symptoms, except a sense of pressure and sensitiveness at the seat of the gall-bladder. When distended, it may, if the abdominal wall is lax and not too thick, be felt as a pear-shaped mass adherent to the liver and moving with it.

In *suppurative cholangitis* the symptoms are usually severe, but may be latent, especially if the disease occurs in the course of an acute infectious disease. They may suggest typhoid.

There is, in most cases, a previous history of gall-stones. The patient usually suffers from irregularly recurring chills, with fever and sweating, the temperature rising to 104° F. or more. There is swelling and tenderness of the liver. Jaundice is always present, but more variable than in the catarrhal variety; it may be intense. Leucocytosis occurs and is suggestive of the condition. Later the case presents the appearance of a well-marked general pyemia with emaciation and weakness.

In *chronic catarrhal cholangitis* the symptoms may be very characteristic. The jaundice may vary if the degree of obstruction alters, as it often does when a gall-stone is situated in the ampulla of Vater, where it may act as a "ball-valve," producing complete obstruction as it moves into the outlet of the duct, and, again, allowing bile to pass as it moves back into the ampulla. In chronic cholangitis there are often recurrent attacks of fever with chills and sweating,—the

so-called intermittent hepatic fever. Such cases may have a history extending through some years.

Diagnosis.—In acute catarrhal cholangitis the diagnosis is usually easily made from the digestive disturbance and gradual onset of the jaundice. Gall-stones are excluded by the absence of colic and the fact that the jaundice is not of sudden development.

In catarrhal cholecystitis there is enlargement of the gall-bladder, which may be palpable as a pyriform tumor adherent to the liver and rising and falling with respiration. Not infrequently a tongue-like lobe of the liver is mistaken for a distended gall-bladder. So may be also a movable kidney; it is usually more easily displaced, and is not attached to the liver. Instead of being smooth, rounded, and elastic, the distended gall-bladder may, from inflammatory thickening, seem more like a solid tumor and be mistaken for cancer in this situation, but cancer is usually associated with jaundice and cachexia. Echinococcic cysts have also to be excluded. The history, shape of the tumor, and laboratory tests for echinococcosis will usually suffice to differentiate the two conditions.

No gall-bladder examination is complete without a roentgenoscopic examination of the stomach and duodenum and a roentgenographic examination when possible, because the filling defects caused by adhesions and pressure from a distended gall-bladder very markedly increase the percentage of diagnosis of gall-bladder disease. Belden (*Amer. Jour. of Roentg.*, Jan., 1926).

The diagnosis of suppurative cholangitis is to be made by a history of gall-stones, the occurrence of a

septic condition with enlargement and tenderness of the liver, and the existence of leucocytosis. There is progressive loss of flesh and strength. The duration rarely exceeds a few weeks, the cases lasting months and ultimately recovering being most probably cases of chronic catarrhal cholangitis due to obstruction, and causing intermittent hepatic fever.

Clinical differentiation of *acute gall-bladder perforation* from acute appendicitis or duodenal perforation is not possible. The symptoms are acute pain near the gall-bladder followed in 2 or 3 hours by referred pain at the umbilicus. In both of the author's cases, in women 22 and 51 years old, the cystic duct was probably obstructed. In 1 there were no stones; in the other, 2 stones of marble size were found in the gall-bladder. In both, the organ showed a pin-point opening. Recovery followed **cholecystectomy** and **multiple drainage**. L. Frank (Internat. Jour. of Surg., May, 1922).

Etiology.—Inflammation of the bile-passages usually results from extension of an inflammatory process from the duodenum, and is, in the majority of cases, associated with gall-stones. The duodenal catarrh that precedes the cholangitis usually follows acute indigestion.

The young are most susceptible to it, but it may occur at any age. It occurs also as the result of exposure to cold, chills, malaria, typhoid fever, pneumonia, and in the course of Bright's disease, chronic heart disease, emphysema, etc. It may occur in the course of any organic liver disease, as inflammation, cancer, or hydatids.

Four cases of acute *typhoid* cholecystitis, 3 developing during and the fourth immediately after the attack. The symptoms were not different from those in other cases. Two patients re-

covered under operative treatment. Söderlung (Upsala Läk. Forh., Sept., 1921).

Infection is generally believed to enter the gall-bladder and ducts by way of the blood stream and lymphatics. Mann, of the Mayo Clinic, has been able to produce a specific cholecystitis by introducing chemicals into the blood. The disturbance is sometimes favored by congestion of the liver, such as may occur during pregnancy.

Chronic catarrhal cholangitis may possibly be a sequel to the acute. It is always due to obstruction of the common bile-duct from gall-stones, stricture, pressure from without, etc. The obstruction may be complete, in which case the ducts are greatly dilated and filled with clear, watery fluid similar to that of dropsy of the gall-bladder. If the obstruction is incomplete, there is less dilatation of the ducts, and, as some bile filters through, their contents are bile-stained and turbid. The gall-bladder is not much dilated in these cases, obstruction of the cystic duct being necessary to cause great dilatation of it. Gall-stones are usually found in it.

Suppurative cholangitis is usually associated with gall-stones, less frequently with echinococci and round worms. The mucosa, injured by such foreign bodies, becomes more susceptible to invasion by pyogenic organisms, and these are present normally in the intestines and in the lowest part of the common bile-duct.

Morbid Anatomy.—In acute catarrhal cholangitis the lower part of the common bile-duct is usually chiefly, and may be the only part, affected. The inflammation may extend to its larger branches. Post-mortem evi-

dences are slight, as redness and swelling disappear after death. A plug of inspissated mucus may fill the diverticulum of Vater and completely obstruct the flow of bile.

The gall-bladder, when affected, contains a more or less viscid mucous secretion; if there is obstruction of the cystic duct, the bladder becomes distended with fluid, of which it may contain 1 or more pints, usually thin and without bile. The walls of the gall-bladder are thin and shining; but, if the obstruction persist, they may become much thickened.

Attention called to the visible changes in the liver in the region of the gall-bladder, noticeable in many instances (27 out of 46 cases) of chronic cholecystitis. They are either dull gray patches, often of considerable size, or milky white lines of varying length, breadth, prominence and pattern. Even in the absence of all other signs of gall-bladder inflammation, these visible changes in the liver, however slight, can be relied on for the diagnosis of chronic cholecystitis and are an important indication for cholecystectomy. R. E. Weible (Surg., Gyn. and Obst., Jan., 1925).

When the symptoms of gall-bladder disease are such that an operation is indicated, a normal appearing gall-bladder does not mean that the diagnosis was incorrect. The finding of a strawberry mucosa, minute particles of cholesterin on the gauze, and stagnant or stringy bile are evidences of pathology. The disease being in the gall-bladder walls, cholecystectomy is best. Bearse (Boston Med. and Surg. Jour., May 7, 1925).

In suppurative angiocholitis the common duct becomes greatly dilated and its walls much thickened. Similar changes occur in the gall-bladder. Both are distended with pus. Ulceration may occur and perforation into the stomach, colon, or

duodenum, or even into the urinary or respiratory tract. The intrahepatic bile-ducts may be distended with pus,—which is usually bile stained. The suppurative process may extend to the hepatic substance, resulting in abscess formation, or to the portal vein, resulting in pylephlebitis.

The bacteria present in these inflammatory processes are very various. The *Bacillus coli communis* probably plays the most important part, but staphylococci and streptococci are also common. The pneumococcus and typhoid bacillus may be the active agents.

Treatment.—This consists in measures to relieve the gastroduodenal catarrh. During an acute attack the patient should be in bed. Plenty of liquids should be taken, especially the alkaline mineral waters. The bowels should be moved freely, but not immoderately, by the use of calomel followed by salines, such as Carlsbad salts, sodium phosphate, etc. Sodium bicarbonate, with bismuth, may prove useful for the gastric disturbance. Such antiseptics as resorcinol, guaiacal carbonate, and bismuth subsalicylate are likely to be serviceable. Salicylic acid and methenamine may be given in an effort to disinfect the biliary tract.

A large cold rectal enema may be given daily; it is said to stimulate contraction of the gall-bladder and ducts and thus promote expulsion of the obstructing mucus.

A light liquid diet only should be given, as it is easy of digestion and less apt to ferment.

Marked symptomatic relief from Lyon's non-surgical drainage in cases which could not be operated upon, many patients preferring repeated

drainage to operation. Under combined duodenal drainage and removal of foci of infection many cases were clinically cured—though, when a gall-bladder has once given trouble, a flare-up is to be expected at any time. Kiel (Tex. State Jour. of Med., Apr., 1922).

In gastroduodenal catarrhs the gall-bladder symptoms can be held in abeyance by proper **lavage**, diet and medication. Not a few cases benefit as well at Saratoga or Bedford Springs as abroad. An important feature is a constant high specific gravity of the bile, due largely to insufficient **exercise** and **life out-of-doors**. The subject should **walk** several miles a day, or the exercise be obtained in a **gymnasium** or with a physical instructor. While the **opiates** are best in acute sharp pain, the low steady growl with epigastric hyperesthesia can be benefited by **alternate heat and cold**, *e.g.*, by use of live steam from the Kommeral **steam pot** for a few minutes, and then cold, this being alternated over a 20-minute period once or twice a day. Alternate **mustard plasters** and **ice-bags** can accomplish this fairly well. The remedial preparations from which the largest number of patients have claimed benefit are:

(A)

℞ *Sodii oleatis*,
Sodii salicylatis
 āā gr. lxviiij (4.5 Gm.);
Phenolphtha-
lcini gr. xv (1 Gm.);
Mentholis ... gr. v (0.35 Gm.).

Ft. pil; No. L.

Sig.: Take two on arising and retiring, followed by a tumblerful of warm water.

(B)—(1)

℞ *Sodii glycohol-*
atis,
Sodii salicyl-
atis,
Sodii bicarbon-
atis āā gr. iv (0.25 Gm.);
Pancreatini ... gr. viij (0.5 Gm.)

Pone in chart. No. xxiv.

(2)

Glycerini,

Tr. cardomomi

comp. āā f̄jiss (45 c.c.).

M. Sig.: Dissolve one powder in ½ tumbler of water, and when well mixed add a teaspoonful of the mixture. Take this about 15 minutes after each meal.

(C)

Nightly doses of **sodium succinate**, 1 Gm. (15 grains), or its use after meals. A. Bassler (Ther. Gaz., Apr., 1923).

Diathermy is very effective in sub-acute or chronic cholecystitis, with or without calculi. Pain is largely or wholly relieved in these patients, as well as in cases with adhesions or spasm. The electrodes measure 22 x 14 cm., are made of tin, and are firmly held, 1 over the gall-bladder and the other over the back. Thirty-minute treatments are given on successive or alternate days. J. Aimard (Jour. de rad. et d'électr., May, 1923).

In the medical treatment of gall-bladder lesions, **frequent meals**, the drinking of much **water** and **hygienic living** are all of importance. The **diet**, while it should not be rich, should not be so rigorous as to be weakening. Instillation of various drugs, such as **argyrol**, **ichthyol** or **mercurochrome** into the duodenum is advantageous. The drinking of **Carlsbad water**, or the like, seems beneficial, and **glycerin** in teaspoonful doses before meals is often useful. **Phenyl salicylate** and **methenamine** are also of advantage. M. Einhorn (N. Y. Med. Jour., June 6, 1923).

In treating early cases of subacute cholecystitis, attention should be given to any septic focus, and any existing digestive disturbance ameliorated by a **restricted diet** for at least 10 days. If there is flatulent distention or salines have alone been taken for months, the writer orders a few **intestinal douches** on alternate days. On the intervening days **mustard-bran liver packs** are applied, and these are continued every 2d day until the gall-bladder tenderness disappears. A satisfactory daily bowel

evacuation must be secured, if necessary by **aloe** or **phenolphthalein** before dinner and a **saline** in the morning. To prevent biliary stasis, 1 to 2 drams (4 to 8 Gm.) of **magnesium sulphate** is ordered taken in a small quantity of strong **sulphur water**, or in plain water when at home, twice a week 1 hour before breakfast. Frequently, 1 pint (500 c.c.) of strong sulphur water is prescribed daily; likewise a cachet containing **methenamine**, **iridin**, **euonymin**, **colalin** and **leptandrin**. If methenamine irritates the bladder, **sodium salicylate** or **sodium benzoate** may be substituted. If there be hypochlorhydria, **dilute hydrochloric acid** is indicated. W. Bain (Pract., Nov., 1924).

As it is impossible to tell when a gall-stone is beginning to form, it is wise to give all patients with active cholecystitis a diet poor in cholesterol. Aside from cream and egg yolk, brain, liver, sweetbread, kidneys and roe should be avoided, and all animal fats strictly limited. If the patient is thin, **olive oil** should be given before meals, especially if hyperchlorhydria exists. A. F. Hurst (Lancet, May 22, 1926).

Surgical treatment is indicated in suppurative cholangitis and cholecystitis, in acute attacks of gall-stone colic when prolonged several days or where perforation of the bladder or ducts is threatened, and also in chronic cholelithiasis. Delay under these conditions exposes the patient's life.

General indications for surgical treatment expressed as follows: Most cases of cholecystitis and cholangitis are surgical. In chronic cases operation may be performed at any convenient time. In cases of cholecystitis without jaundice, seen during an attack, it is usually best to wait until the attack has subsided. If a severe degree of pancreatitis is suspected, the advisability of operation is questionable. Operation in the presence of jaundice should always be avoided, if possible. Judd (Jour. Kans. State Med. Soc., June, 1921).

A second attack of cholecystitis possibly, and a third one positively, warrants serious consideration of surgical interference. The degree of restoration to normal health is in direct [inverse] proportion to the duration of the disease before operation. J. B. Deaver (Neb. State Med. Jour., June, 1922).

Prompt **cholecystectomy without drainage** in the acute stage of cholecystitis advocated. Two cases were satisfactorily dealt with in this way. The procedure is permissible where the gall-bladder can be removed entire, without escape of contents, and proper ligation, hemostasis and a dry operative field are obtainable. It is advantageous in the prompt recovery, forestalling of adhesions, and avoidance of weakening of the abdominal wall, being analogous to prompt appendectomy in acute appendicitis. Drainage is, on the other hand, required in feeble patients or where adhesions, abscesses or other special conditions are present. A. Chalié (Lyon chir., Jan.-Feb., 1924).

Among 580 cases of biliary tract disease operated on at the Johns Hopkins Hospital between 1889 and 1924, 72 per cent. were cured, 11 per cent. were improved, and 6 per cent. unimproved.

The mortality immediately following operation was 9.5 per cent., the highest percentage—24—falling in the group with stones in the common duct. The gall-bladder was removed in 49 per cent. and drained in 51 per cent. The deaths and the percentage of recurrence of symptoms were much higher after **drainage** than after **cholecystectomy**.

The last-named procedure is therefore preferable, provided the patient's condition is such that the extra time under anesthesia will not too greatly lessen his chances of recovery. A. Blalock (Jour. Amer. Med. Assoc., Dec. 27, 1924).

[See also ABDOMEN, SURGERY OF: SURGICAL DISEASES OF THE LIVER AND BILIARY PASSAGES, Volume I.]

ACUTE EMPYEMA OF THE GALL-BLADDER (ACUTE PHLEGMONOUS CHOLECYSTITIS).—Symptoms.—The onset in this condition is usually sudden, with pain in the right side of the abdomen in its upper part, but, as in appendicitis, the pain may be general over the abdomen.

Nausea, vomiting; a rapid, feeble pulse; thoracic breathing, rise of temperature, prostration, distention, and tenderness of the abdomen are the chief symptoms. In the cases in which the disease is circumscribed, local tenderness soon becomes more marked.

Jaundice is not usually present in these cases. Intestinal symptoms may be marked and not infrequently lead to a diagnosis of acute intestinal obstruction.

Diagnosis.—This is often impossible, especially in the fulminating cases. Acute gall-bladder empyema is most often confounded with gangrenous appendicitis.

In the less severe cases the signs of local disease—as pain, tenderness, signs of exudation, abdominal tension, etc.—may be sufficient to distinguish between the two diseases, unless the appendix is situated abnormally high.

Perforation of the stomach, the duodenum, the colon, the gall-bladder, etc., usually causes greater collapse at first and less marked septic symptoms later.

Etiology.—Acute empyema of the gall-bladder is a relatively rare disease. In about 75 per cent. of cases it is associated with gall-stones. It is due to infection by bacteria, which may gain access by way of the blood or the bile. The typhoid bacillus, the

colon bacillus, the pneumococcus, and the staphylococcus are the organisms most frequently present. Quite a large number of cases have followed typhoid fever, in some instances months after convalescence.

A comparison has been drawn between the causation of this disease and of appendicitis, the gall-bladder affection being of less frequent occurrence on account of its ampler blood-supply.

Morbid Anatomy.—The gall-bladder is distended, but not large, not containing more than a few ounces of mucus. There is a strong tendency to gangrene, proportioned to the virulence of the infection and the tension of the organ.

The course of gall-bladder empyema is rapid, usually within four or five days. Adhesions are early formed to the intestines, omentum, etc. Later, perforation may occur and abscess result, or an abscess may form without perforation. In the severe cases general peritoneal infection is liable to occur. The contents of the gall-bladder may be very fetid.

Treatment.—Acute empyema of the gall-bladder is so rapidly fatal that only prompt measures are successful. As in phlegmonous appendicitis, so here **prompt surgical treatment** is necessary. The real difficulty is in making the diagnosis. In the early stage care should be taken not to obscure the symptoms by the undue use of opium.

The temporary measures to be applied should consist of **absolute rest, hot applications, complete abstinence from food, water only** being given by the mouth, and **relief of symptoms** as far as possible until the necessity for operation is established, when the

gall-bladder, if there is empyema or gangrene of it, should be **incised** and **drained** or **removed**. In milder cases, in which the disease is localized, it is probably wiser to delay operation until the disease has been well circumscribed by the inflammatory process, when **incision** and **drainage** may be carried out and **gall-stones**, if present, **removed**.

TUMORS OF THE BILIARY TRACT.

CANCER.—Cancer may occur as a primary disease of the gall-bladder and of the bile-ducts or may be secondary to cancer of the liver, stomach, pancreas, or peritoneum.

Primary cancer of the gall-bladder affects females much oftener than males—in the ratio of 3 or 4 to 1. The bile-ducts are affected about equally in the two sexes. The disease occurs usually from 40 to 70, but occasional cases are met with in early life and at advanced age.

Gall-stones are present in practically all cases of cancer of the gall-bladder. The relationship between the two conditions is in dispute. Some regard the cancer as developing in the glands of the mucosa on account of the irritation by the calculi, while others look upon them as formed subsequently to the commencement of the cancer. The greater frequency of occurrence of gall-stones in females gives support to the view that their irritation frequently excites the development of cancer.

The disease usually begins at the fundus of the gall-bladder, and at either extremity of the common bile-duct.

CANCER OF THE BILE-DUCTS.

—**Symptoms.**—It rarely forms a

tumor that can be felt through the abdominal wall. The jaundice usually occurs early, and is intense and persistent. The stools are persistently clay colored. A fatal termination usually follows in three or four months, from cholemia. It may be the cause of cholangitis with intermittent hepatic fever or there may be suppurative cholangitis.

It is practically impossible to make a positive diagnosis without an exploratory operation. The persistent intense jaundice is suggestive, and may, in some cases, render the diagnosis extremely probable, especially in the absence of biliary colic. The most valuable diagnostic indication is *Courvoisier's sign*, i.e., enlargement of the gall-bladder with jaundice.

Morbid Anatomy.—The cancer usually develops in the circumference of the duct as an infiltration of the sub-mucous tissue. The surface of the deposits may be smooth or ulcerated. They occur most frequently in the diverticulum of Vater and may extend to the duodenal papilla.

Treatment.—In any case of long-standing grave icterus, **surgical treatment** is indicated, whether Courvoisier's sign is present or not; if a common-duct stone is found, it can be removed, whereas if cancer is found, especially about the papilla of Vater, the radical operation can be proceeded with, or, if the patient's condition does not permit, further operation may be delayed for a later sitting in a day or two. In early cases without metastasis, good results are obtained by **excising the tumor area**, including the papilla of Vater, and performing a **cholecystenterostomy**; in inoperable cases **cholecystostomy** will prolong life an average of $\frac{1}{2}$ year (Morian).

Case of primary carcinoma of the common duct at the junction of the hepatic and cystic ducts. The patient had had gastric upsets and increasing jaundice for 2 months. At operation the growth, of cherry size, dilating the hepatic duct, was removed, the hepatic duct joined to the common duct, and a T-tube introduced for 3 weeks, with ultimate recovery after several brief attacks of icterus. The writer preferred the above procedure in this case to hepatico-enterostomy, which might have led to ascending infection. Eighteen months later, recurrence had not taken place. Amberger (*Arch. f. klin. Chir.*, Oct. 17, 1921).

CANCER OF THE GALL-BLADDER.—Symptoms.

—Not rarely the attention is first arrested by the accidental discovery of a smooth, firm, egg-shaped swelling below the costal margin. It is fixed to the liver and moves with it in respiration. There is usually a sense of discomfort and later often of irregular pain in the neighborhood of the mass. The pain is rarely persistent or severe, and may disappear altogether. It is usually worse at night and may extend around to the back. Later, as the tumor enlarges, it becomes less defined, and nodules often appear on its surface. If dissemination has occurred, nodules may be felt on the liver and in the peritoneum. Ascites may result from the peritoneal affection or from pressure by diseased lymph-glands on the portal vein in the hilum of the liver. Jaundice occurs in probably not more than half of the cases; when it occurs it is a late symptom and depends on pressure on the bile-ducts in the hilum.

There is usually early general failure of health. In the later stages there is marked cachexia, and loss of flesh and strength, with, not infre-

quently, mental weakness and a prolonged period of subdelirium. Adhesions to the intestines may give rise to symptoms of partial or complete obstruction. Blood-stools may also occur.

The course is usually rapid, death occurring in a few months after the appearance of the tumor.

Twenty cases of primary cancer of the gall-bladder were observed among 525 operations on the gall-bladder and biliary passages—a percentage of 3.8. In 10 of these cases stones were demonstrated, and they were suspected to be present in others, the gall-bladder being, however, so involved in the tumor that they could not be shown. Investigations of others seem to indicate the presence of gall-stones in 70 to 95 per cent. of cases of primary cancer. Waits (*Va. Med. Mthly*, July, 1922).

Diagnosis.—The presence of a tumor and the progressive character of the local and general symptoms of the disease usually suffice for a diagnosis. In the absence of a tumor the diagnosis is difficult and may be impossible, as it may be also to distinguish a tumor formed by matted intestine from local peritonitis from a tumor of the gall-bladder. Even incision and exploration not rarely fail to clear up the difficulty.

Tumors of the pylorus, of the transverse colon, of the kidney, and of the suprarenal gland may simulate tumor of the gall-bladder.

Morbid Anatomy.—The cancer may begin at the fundus or near the cystic duct, but often the walls of the gall-bladder are found uniformly thickened. The diseased gall-bladder may form a large, smooth or nodular mass adherent to the liver and to the intestines, and in the center of the mass a considerable cavity filled with

opaque gray fluid containing much flocculent material and several gall-stones. The cancer is usually a cylindrical epithelioma, but it varies much. It may extend into the liver directly or by way of the portal fissure, where it may affect the portal vein and give rise to multiple deposits in the liver. The lymph-glands in the hilum of the liver are usually affected.

Treatment.—Symptomatic treatment is usually all that can be carried out. If the disease is recognized early before it has affected neighboring structures **cholecystectomy** may be practicable. Mayo Robson reports such a case in which he removed a large portion of the right lobe of the liver with the gall-bladder. The patient made a good recovery. Other similar cases have been reported.

W. J. Mayo has emphasized gall-stones as the most important etiological factor in malignant disease of the gall-bladder, and advises early operation, other things being equal, on active gall-stones, since nearly all the mortality-giving complications are the result of delay.

OTHER TUMORS OF THE BILE-DUCTS are rare. Fibromata have been met with. Adenomata occur occasionally. I met with one of the diverticulum of the common duct in a man aged 50 years. A gradually increasing jaundice was the first symptom. Later suppurative cholangitis occurred, with chills, high fever, and tender liver. At the autopsy the mass in the duct was found to act like a ball-valve, obstructing the discharge of bile.

Benign tumors of the gall-bladder (papilloma and adenoma especially) occurred in a Mayo series once in every 23 cases of cholecystectomy, and once in every 36 cases in the writer's

series. The invariable presence of chronic inflammatory changes in gall-bladders containing such tumors emphasizes the importance of chronic irritation as a factor. I. Abell (Ann. of Surg., Mar., 1923).

HYDROPS OF THE GALL-BLADDER.

Two forms of hydrops due to occlusion of the cystic duct are recognized by Daniel and Babès: The *transudative* or *serous* and the *secretory* or *mucous*. In the former, the gall-bladder is fibrotic; in the latter, its mucosa shows inflammatory lesions and the obstruction is more recent. The absence of bile is due to reabsorption of the bile pigment and salts by the gall-bladder mucosa or to precipitation in the form of calculi.

In *cystic dilatation of the common duct*, mechanical obstruction seldom causes dilatation beyond the diameter of the small intestine, and the dilated structure always exhibits the cylindrical form of the duct. Simple drainage of a cyst exerting pressure on the duct is insufficient to effect a cure, 21 out of 32 cases thus treated dying within a few days after operation. Of the remaining 11 cases, 5 recovered—2 following a primary **choleodocho-enterostomy**, and 3, after **drainage** followed by choleodocho-enterostomy. P. J. Reel and N. E. Burrell (Ann. of Surg., Feb., 1922).

Inertia of the gall-bladder is a clinical entity. The organ is distended and there is tenderness in recumbency, with dyspeptic phenomena and also migraine with bilious vomiting. The condition appears mainly due to disturbance of the vegetative nervous system. The treatment consists of repeated **non-surgical drainage** of the bile, together with **pilocarpine** or **physostigmine** by the mouth or subcutaneously, or **pituitary extract**. Chiray, Pavel and Milochevitch (Presse méd., Sept. 12, 1925).

ALEXANDER MCPHERAN,
Toronto.

LIVER, GALL-BLADDER, AND BILE-DUCTS, SURGERY OF. See ABDOMEN, SURGERY OF, and ABDOMINAL INJURIES.

LOBELIA.—Lobelia consists of the dried leaves and tops of the *Lobelia inflata*, or Indian tobacco, a weed indigenous to the United States, collected after a portion of the capsules have become inflated. The plant is a small herb, with alternate leaves; an erect, hairy stem, and blue flowers in the axils of the leaves. It has a slightly irritating odor and a burning, tobacco-like taste. It contains alkaloids, constituting the amorphous *lobeline*, and an acid, *lobelic acid*; gum resin, fixed oil, lignin, salts, chlorophyll, and a volatile oil.

A pure, crystalline form of lobeline was isolated by Wieland in 1918 from among other, much weaker lobelia bases, and has been availed of clinically.

PREPARATIONS AND DOSE.—

Lobelia, U. S. P. (lobelia). Dose, 1 to 8 grains (0.065 to 0.5 Gm.); official average dose, 1½ grains (0.1 Gm.).

Tinctura lobeliae, U. S. P. (tincture of lobelia), is a 10 per cent. preparation. Dose, 10 to 60 minims (0.6 to 4 c.c.).

Fluidextractum lobeliae, N. F. (fluidextract of lobelia), is a 100 per cent. preparation. Dose, 1 to 8 minims (0.06 to 0.5 c.c.).

Crystalline lobeline ("alpha-lobeline"), unofficial. Dose, in adults, ¼ grain (0.01 Gm.), and in infants, ⅓₂₀ grain (0.003 Gm.), subcutaneously or intramuscularly. In adults, slow intravenous injection of ⅓₂₀ grain is asserted to be feasible.

PHYSIOLOGICAL ACTION.—Lobeline, the amorphous active agent of lobelia, exerts almost precisely the same effects as nicotine, the alkaloid of tobacco. Lobelia causes a brief primary stimulation of the motor centers in the spinal cord and medulla, in the latter acting especially upon the respiratory and vomiting centers. This stimulation is soon followed by depression, and with large doses paralysis.

A relatively important feature of the physiological action of the drug is that in the secondary depressive stage the motor nerve-endings in involuntary muscles are also involved, and, in particular, the endings of the vagus in the bronchi. This last effect is especially perceptible where the bronchioles are abnormally constricted (as in bronchial asthma) at the time when the drug is administered, and affords one of the chief therapeutic uses of lobelia. The drug also tends to increase the secretions of the respiratory mucous membranes.

Upon the circulation lobelia likewise resembles nicotine in its action. It tends to paralyze the cardiac branches of the vagi (Dreser), and small doses taken continuously tend to cause a persistent increase in the pulse rate (Sollmann).

The crystalline lobeline isolated by Wieland is stated to be devoid of the properties of depressing the vagus endings in the bronchi and of producing emesis. On the contrary, large doses of it stimulate the vagus center and induce slowing of the pulse and bronchial spasm. Its outstanding action in smaller doses, however, is to stimulate the respiratory center. In cats, after respiration had been partly or wholly stopped by a mixture of carbon monoxide and air, and fresh air thereupon allowed had failed to improve the breathing, intravenous injection of 0.002 Gm. (⅓₂₂ grain) of alpha-lobeline was at once followed by increased frequency and amplitude of respiration and saved the animal's life in each of 12 experiments (K. Peters).

POISONING.—The symptoms of poisoning by lobelia or amorphous lobeline are much the same as those of tobacco poisoning. Nausea, giddiness, faintness, trembling of the limbs, cold sweats, frequent and prolonged vomiting accompanied by intense prostration, violent abdominal and esophageal pains, with occasional purging, are the chief features. The pulse becomes almost imperceptible; the breathing, shallow and difficult. The vision is affected. Stupor is followed by coma or convulsions, more or less widespread paralysis, collapse, and death by paralysis of respiration. Vomiting is occasionally absent; the constitutional symptoms are then accentuated, and death is apt to follow. One dram of the powdered leaves has proved fatal in about thirty-six hours. On post-mortem examination the brain was found congested and the gastric mucous membrane inflamed.

Treatment of Lobelia Poisoning.—This consists in washing out the stomach by siphonage. Solutions of tannic or gallic acid may be given, followed by hypodermic injections of stimulants, such as ether, ammonia, strychnine, and digitalis. Saline hypodermoclysis, with or without the addition of epinephrin, may also be availed of. The recumbent position should be maintained, and heat applied to the extremities.

Opium given in full doses will relieve the pain, and later, in moderate doses, control the vomiting.

THERAPEUTICS.—Lobelia is chiefly used for the relief of **asthma** of the **bronchial** or **gastric form**. The drug should be taken in doses of $\frac{1}{2}$ to 1 fluidram (2 to 4 c.c.) of the tincture at the beginning of the attack, or in 10-drop doses every quarter of an hour until nausea appears or relief is obtained. It is a frequent constituent of unofficial asthma powders or cigarettes, to be burned or smoked during the asthmatic attacks. A feeble heart contraindicates its use.

Children are more tolerant of lobelia than adults.

Other spasmodic affections have been treated with lobelia,—**pertussis**, **spasmodic croup**, **chorea**, **epilepsy**, **infantile convulsions**, and **tetanus**—but in many instances other remedies, equally efficacious and less dangerous, are to be preferred.

In **bronchitic cough** with scanty expectoration and **bronchial spasm** lobelia may be useful as a depressing expectorant.

By some, lobelia has been used for overcoming **rigidity of the os** during labor.

Lobelia in an infusion (1 ounce to the pint) has been deemed useful as a lotion in the treatment of the **dermatitis** due to poison ivy (*Rhus toxicodendron*).

Lobelia should not be employed as an emetic, as it produces too much nausea and depression. It has caused death when thus used.

Crystalline lobeline is indicated, according to K. Peters (Med. Jour. and Rec., Mar. 18, 1925), in all forms of central respiratory depression, partial or complete. The effect continues for $\frac{1}{2}$ to $1\frac{1}{2}$ hours and is not cumulative, so that the drug can be repeated or prolonged infusion of it carried out. Clinically the remedy has been used in **poisoning by narcotics**, **collapse in diphtheria**, **asphyxia neonatorum**, and for imprisoned miners. Indications specifically mentioned comprise **poisoning by ether**, **chloroform**, **morphine** or **carbon monoxide**, **acidosis** with respiratory disturbance, and **collapse** in various diseases, **drowning**, and **surgical shock**. The drug is not indicated, however, in dyspnea, for here the respiratory center is already reacting to its physiologic stimulus, carbon dioxide. W. and S.

LOCAL ANESTHESIA. See VARIOUS ANESTHETICS.

LOCOMOTOR ATAXIA. See TABES DORSALIS.

LUDWIG'S ANGINA. See PHARYNX AND TONSILS, DISEASES OF.

LUMBAR PUNCTURE.—This operation was originally proposed by Quincke for the withdrawal of cerebrospinal fluid from the spinal canal, and is used for diagnostic and therapeutic purposes. Its diagnostic uses are to estimate the pressure of the cerebrospinal fluid and also to determine its characteristics and composition by subsequent physical, chemical, microscopical, and bacteriological examination. Its therapeutic uses are as a decompressive agent in meningitis, hydrocephalus, intracranial tumors, cerebral abscess, uremia, etc., for the purpose of administering antitoxic sera in tetanus and cerebrospinal meningitis, and for the purpose of inducing spinal anesthesia. Temporary diminution of intracranial and intraspinal pressure may be obtained in the diseases mentioned by the withdrawal of small amounts of fluid from the spinal canal, because the spaces in the brain and that of the spinal column are continuous.

ANATOMY.—The spinous processes in the lumbar region of the vertebral column do not project downward as much as in the other parts and a distinct space of about $\frac{7}{8}$ inch (22 mm.) exists in the transverse, and $\frac{3}{8}$ inch (15 mm.) in the vertical, diameter between the vertical arches, which is filled with ligaments that will allow the passage of a needle. The lower limit of the spinal cord is the second lumbar vertebra. A puncture may be made below that point, under rigid asepsis, with slight risk.

INSTRUMENTS REQUIRED.—A special stylet needle, $3\frac{1}{2}$ inches (9 cm.) long and $\frac{1}{25}$ inch (1 mm.) in outside diameter (gauge No. 19) with short point, a scalpel, a sterilized graduated test-tube, culture tubes, an ordinary hydrometer, and if the cerebrospinal pressure is desired a small mercurial manometer or water manometer.

LOCATION OF PUNCTURE.—The puncture is usually made between the third and fourth or between the fourth and fifth lumbar vertebrae, but may for diagnostic

purposes be made between the fifth lumbar and the first sacral. The needle is inserted at a point just below the tip of the spinous process and in the median line. The spinous process may be located by counting down from the seventh cervical vertebra, or by passing a transverse line between the highest points of the iliac crests, the patient standing, which will mark the tip of the spinous process of the fourth lumbar vertebra. The patient may sit in a chair or lie on his left side; in either case the body must be bent forward in an arch, knees drawn up, and shoulders forward. The site of the puncture and the operator's hands must be sterilized, and the needle boiled. In a majority of instances (especially in tabes or paresis), anesthesia is unnecessary. Otherwise, infiltration anesthesia of the skin and to the depth of a hypodermic needle with 1 per cent. eucaïne or cocaine solution will suffice in adults; in children a little ether may be necessary.

TECHNIQUE.—The site of puncture is aseptitized with 10 per cent. tincture of iodine, which may be preceded, if desired, by scrubbing with green soap and washing with alcohol and ether. With the operator's left thumb or index finger between the two spinous processes as a guide, the needle is inserted on the level of the finger, usually in the median line, in an upward and inward direction. In an adult it will enter the spinal canal at a depth of from $2\frac{1}{2}$ to 3 inches (6 to 7.5 cm.); in a child, at from $\frac{3}{4}$ to $1\frac{1}{2}$ inches (2 to 4 cm.). If bone is encountered, slightly withdraw the needle and then reinsert it in a slightly different direction.

When the canal is entered, withdraw the stylet, and collect the fluid, as it drops from the needle, in a sterile test-tube. Discard the first few drops, if they are blood-stained. Not more than $\frac{1}{2}$ ounce (15 c.c.) of fluid (preferably 5 to 10 c.c.) should be withdrawn in case of an adult, not more than $1\frac{1}{4}$ drams (5 c.c.) in case of a child; except when puncture is made to relieve intracranial pressure, when from 1 to $1\frac{1}{2}$ ounces (30 to 45 c.c.) may be removed if necessary.

It is wise to keep the patient in bed for 18 to 24 hours after puncture. Post-puncture headache from reduced cerebrospinal pressure may be relieved by pituitary ex-

tract or intravenous injection of 0.5 per cent. salt solution (100 c.c.).

Lumbar puncture needles on the market are as a rule not smaller than No. 20 gauge, and more often No. 14 to No. 18. Puncture of an ambulatory patient with a needle of this size will result in headache in a large percentage of cases, due to leakage of spinal fluid because of destruction of the longitudinal fibers composing the dural sac and of the endothelial covering. The writer advocates the use of a No. 23 gauge needle of soft-tempered steel, with round-pointed, though sufficiently sharp point. Aspiration is required when a small-calibered needle is used; the author never found aspiration followed by untoward symptoms. H. M. Greene (Northwest Med., July, 1923).

ADMINISTRATION OF SERA.—For this purpose a syringe with a capacity of at least 1 ounce (30 c.c.) is required. Cerebrospinal fluid equal to the amount of serum to be injected is first withdrawn; the serum is slightly warmed and then slowly injected through the needle.

In tetanus from 10,000 to 12,000 units of antitetanic serum are injected into the subdural space, and at times into the nerves of the brachial plexus, if the infected site is upon the upper extremity, and also intravenously.

In cerebrospinal meningitis, amounts up to 1 or $1\frac{1}{2}$ ounces (30 to 45 c.c.) of serum are injected into the third or fourth lumbar space, after a like amount of cerebrospinal fluid has been withdrawn. According to Sophian, the blood-pressure is a valuable gauge of the safe amount of fluid withdrawal and serum injection, a total drop of 20 mm. Hg not being exceeded. The injections are repeated, at intervals of from 12 to 24 hours, for 3 or 4 days. Return of symptoms demands a renewed course of injections.

W.

LUMINAL. See PHENOBARBITAL.

LUNGS, DISEASES OF THE.

—The more important diseases of the lungs—bronchopneumonia, croupous pneumonia, asthma, etc.—are treated in full under their respective headings.

PULMONARY CONGESTION.

Congestion of the lungs typifies the hyperemia observed elsewhere in the organism, and may, therefore, be divided into two classes: active and passive.

ACTIVE CONGESTION OF THE LUNGS.

SYMPTOMS.—The symptoms vary with the intensity of the congestion and the amount of lung-tissue involved. Dyspnea, cough, frothy expectoration, localized pain, wheezing, and accelerated breathing, owing to diminution of the caliber of the air-cells and deficient oxygenation, are usually observed; occasionally the expectoration is tinged with blood. In rare cases there is active pulmonary hemorrhage, followed by death. All these symptoms may be observed in pulmonary congestion of malarial and gouty origin. Death may also occur as the result of asphyxia, brought on by the mechanical blocking of the tubes by excess of secretion. The temperature rarely surpasses 100° F., and the pulse is tense and bounding. In favorable cases deferescence usually begins twenty-four to thirty-six hours after the onset of the active symptoms.

Both lungs are usually involved, and in mild cases the hyperemia gives rise to appreciable signs only at the base. Fine fremitus may be detected on palpation; the breath-sounds are bronchovesicular and unusually audible, the expiration being prolonged and harsh. Moist, subcrepitant râles attend the more severe cases, but these are also most evident toward the bases.

ETIOLOGY AND PATHOLOGY.

—Active congestion may occur as a

primary disorder, especially in persons in whom the kidneys are diseased. Exposure to damp and cold air while the surface is warm, as is the case during bicycle-riding, or prolonged bathing in cold water may under these conditions bring on pulmonary hyperemia, which in rare cases assumes a grave form. In the vast majority of cases, however, active pulmonary congestion is due—not to speak of the conditions such as pneumonia, pleurisy, bronchitis, etc., of which it forms an early stage—to the inhalation of steam, hot air, and other irritating factors. It has also followed violent emotions or fright. In the latter case paresis of the vasomotors is probably the most important pathological feature.

Congestion of the bronchial mucous membrane and the alveolar walls, and the presence of bloody and frothy mucus on section, constitute about all the morbid conditions found *post mortem*. The alveolar epithelium is sometimes found granular and swollen.

TREATMENT.—In cases due to exposure **dry cups**, **mustard foot-baths**, and **opium** internally, followed by a **saline purgative**, usually suffice to overcome the hyperemia when it is not severe. In cases brought on by local irritants—steam, hot air, acid fumes, etc.—the **bromides** in large doses are very effective. When the dyspnea is severe, however, **venesection** is indicated, especially if the patient be large and plethoric: a class of individuals in which active congestion is apt to occur. **Wet cups** should be used if venesection cannot be resorted to. **Tincture of veratrum viride** or of **aconite** in small, but frequently repeated doses, and closely

watched, will then prove effective in maintaining the pulmonary circulation at its normal level. **Nitroglycerin**, by dilating the vascular tree, tends greatly to relieve the pulmonary congestion. **Morphine** is of great value to relieve the dyspnea and pain. When there is any doubt as to the possible presence of pneumonia, **creosote carbonate**, in 5-minim (0.3 Gm.) doses, in capsules, should be given every three hours.

PASSIVE CONGESTION OF THE LUNGS.

The passive form is generally due to cardiac diseases, especially those in which the mitral and tricuspid valves are involved, and when dilatation and fatty degeneration are present. It may also occur as a complication of cerebral lesions and as a result of asphyxia. Tumors may also give rise to passive congestion by pressing upon a large venous trunk. Briefly, it may be caused by any condition capable of damming back the blood in the lungs.

SYMPTOMS.—The symptoms of this condition do not vary greatly from those of active congestion, but they do not appear suddenly, the progress of the pulmonary disorder depending upon that of the causative affection. In heart disease, for instance, the dyspnea only appears when compensation begins to fail. In pulmonary tumor active symptoms only occur when the pressure of the neoplasm is sufficient to cause a degree of vascular stenosis for which collateral circulation cannot compensate. Cough and the expectoration of frothy and blood-stained serum, which upon examination is found to contain pigmented alveolar epithelial

cells, constitute the characteristic signs of this form of hyperemia.

ETIOLOGY AND PATHOLOGY.

—The congestion being due to mechanical impediment to the flow of blood through the vessels, the latter are distended and the whole lung is enlarged. The vascular engorgement, the blood being dark and venous, causes the pulmonary tissue to become erect, firm, and resisting. When cut, it appears reddish brown; hence the name "*brown induration*" often given to this condition. There is marked increase of the connective-tissue elements and distention of the smaller vessels and alveolar capillaries, edema being commonly present. The alveolar walls are filled with cells containing altered blood-pigment, while their cavity contains epithelial cells in various stages of metamorphosis.

The morbid process starts at the base and gradually extends upward until, in some instances, the entire lung is involved.

TREATMENT.—The treatment is obviously that of the causative disorder: a **change of posture** from dorsal to lateral or even ventral sometimes affords relief temporarily. If possible, the patient should **avoid** the **recumbent position**, and the condition may be greatly improved by **free venesection**.

When bleeding cannot be resorted to, **veratrum viride**, 5 minims (0.3 c.c.) every ten minutes until the pulse softens, then every hour, is sometimes very effective by causing dilatation of the vessels of the splanchnic area. In desperate cases **aspiration** of the **right auricle** may be tried when blood cannot be obtained from the arm.

HYPOSTATIC CONGESTION.

This is a form of passive congestion in which the blood accumulates in the posterior and inferior portion of one or both lungs, as a result of great prostration and debility.

SYMPTOMS.—As noted by Piorry, hypostatic congestion may be suspected when old and debilitated patients, contrary to their custom, sleep with opened mouth. This suspicion becomes confirmed when slight cyanosis indicates that proper oxygenation of the blood is not taking place. Edema of the lower extremities is observed late in the history of the disease. In a large proportion of the cases, however, these characteristic symptoms are not detectable, and the diagnosis has to be based upon the physical symptoms. Slight dullness at the base of the lungs, feebleness of the respiratory murmur, and moist râles are the most marked of these, and suggest the presence of hypostatic congestion when other active symptoms attending inflammatory disorders of the lung are not present.

ETIOLOGY AND PATHOLOGY.—This form of congestion is generally observed in elderly people who are obliged, through disease, to remain a long while in the dorsal position. The shoulders being raised by the pillows, the blood normally accumulates in the bases. Chronic diseases, long-continued fevers, and cardiac disease attended by weakness of the heart-muscle may thus favor the development of the disease. Fractured limbs in the aged may also prove indirectly causative if the patient is allowed to remain in bed beyond a certain time. The lesions resemble those of a mild lobular

pneumonia. The capillaries are enlarged, the air-cells more or less collapsed, and the lung-tissue is dark red, dense, and engorged with blood and serum: a condition which has been termed "splenization."

TREATMENT.—The prevention of hypostatic congestion should be an important feature of the measures adopted in cases of paralysis, protracted tuberculosis, cancer, fracture, typhoid fever, etc., especially when these occur in old subjects. The posture should be frequently changed not only from side to side, but also in respect to the elevation of the shoulders. The **semiprone position**—the patient lying with one side of his abdomen touching the bed—is a useful one to prevent or relieve the local engorgement, but he should be allowed to leave his bed as soon as at all practicable.

It is important to sustain cardiac action; this may best be done by means of **strychnine, nitroglycerin, caffeine, digitalis, or pituitary gland.** Two grains (0.13 Gm.) of the latter with $\frac{1}{40}$ grain (0.0016 Gm.) of strychnine every four hours are valuable in such cases.

PULMONARY ABSCESS.

Although abscess of the lung is almost always associated with pulmonary tuberculosis and rarely with lobar pneumonia, it may also be the result of other local or neighboring pathological processes and injuries.

Mechanical injuries, such as fractured ribs and penetrating wounds, may cause abscess of the lung, especially in cases in which the vitality and, therefore, resistance to bacterial growth are below normal. Gangrene as a complication of pulmonary ab-

scess has been considered under CHEST, INJURIES OF, in the third volume.

SYMPTOMS AND DIAGNOSIS.

—When, in the course of pyemia or any other infectious disease in which the lungs are not primarily involved, localized distress in one or both lungs, shortness of breath, etc., and a rise in temperature appear, abscess of the lung is a possibility. It can only be verified, however, by the presence of pus in the sputa. These are usually yellowish green and emit an offensive odor, though less so than in gangrene or putrid bronchitis. At times they assume a reddish or brownish tinge and contain shreds of tissue which, microscopically examined, often prove to be elastic fibers. Blood-corpuscles, alveolar epithelium, crystals of margarín, cholesterin, mold-fungi, and various bacteria, according to the causative malady, may also be found in the secretions. Chills and suppurative fever are often present. There is a leucocytosis.

In abscess occurring as complication of acute pneumonia there is an intermittent rise in the temperature, usually about the time of the crisis, and marked prostration appears. At first physical examination affords but little information, though the signs of consolidation persist. When an abscess of large size opens into the bronchi, however, the signs of a cavity present themselves.

An X-ray study is advisable. Injection of iodized oil through the glottis or by the intercricothyroid route is useful in demonstrating the focus of supurations.

The history is of diagnostic value. Previous pneumonia or septicopyemia would be strongly corroborative.

Tuberculosis is differentiated by its history, the smaller amount of pus in the sputum, and the usual sputum tests.

ETIOLOGY.—Acute pneumonia (lobar and lobular) is the disease in the course of which pulmonary abscess most frequently occurs next to pulmonary tuberculosis, but, at best, even here it is not a frequent complication, suppurative infiltration being the rule, and when abscess does occur it is usually comparatively small and multiple. Abscess is, however, a frequent sequela in all forms of inhalation and deglutition bronchopneumonia. Septicemia or pyemia may also be accompanied by abscess of the lung through infectious emboli. It is especially liable to occur in persons in whom the general health had been poor before the onset of the causative affection, and in lymphatic or alcoholic subjects.

In some forms of bronchopneumonia it is said to be frequently observed. It occasionally presents itself as a complication of abscesses in neighboring structures, the liver particularly; the pleural cavity, and of tumors and cysts.

PATHOLOGY.—The local lesions are merely those of an ordinary abscess, containing micro-organisms, these varying, as stated, with the nature of the causative disease. Streptococci, the *Diplococcus pneumoniae*, and Friedländer's bacillus among others have been observed. The most frequent location (80 per cent.) is in the lower lobes. The size of the abscess may vary greatly from that of a chestnut to that of a large orange. The walls of the abscess are irregular and shreddy. An abscess of long duration shows a dense limiting

peripheral membrane, and closed abscesses considerable cicatricial tissue: a clear indication of the tendency to resolution of these abscesses if the general health can be improved. Pulmonary abscesses may rupture into the pleura, pericardium, or peritoneum.

PROGNOSIS.—The prognosis of non-tuberculous pulmonary abscess has improved since the introduction of the newer therapeutic measures. In abscess complicating pneumonia the prognosis is not as unfavorable as would logically appear. The prognosis becomes unfavorable, however, when pulmonary abscess occurs as a complication of abscesses elsewhere.

TREATMENT.—An important therapeutic indication is to support the patient's strength by the use of tonics and stimulants and by **forced feeding** with light and easily digested foods. Inhalation of antiseptic **sprays** (thymol, phenol, creosote) is beneficial. In non-tuberculous cases the abscess, when superficially located, may be evacuated by **aspiration** or **incision** when the diagnosis is certain and the condition refractory to other measures.

Bronchoscopic treatment is strongly recommended by Jackson and **artificial pneumothorax** by Tewksbury.

Brulé and Hillemand urge that, when the nature of the lesion is obscure, **emetine** be tried.

Recovery depends on **drainage**, either by natural or surgical measures. Acute multiple abscesses cannot drain and always cause death. Aspiration abscesses, regardless of their size, may drain through the bronchus, cicatrize, and become obliterated. Medical treatment consists of **forced feeding, rest, sunshine, open air, and alkalinization**. When no further improvement can be effected, or if retrogression occurs, **operation** is advisable. Of 16 patients

operated on by Hedblom, 3 died, a mortality of 18.7 per cent. Norris and Landis give the mortality of unoperated cases as 50 per cent. W. S. Lemon (Can. Med. Assoc. Jour., x, 1079, 1920).

Out of 14 abscess cases in which **resection of a single lobe** of the lung was carried out, 6 died, while out of 7 similar unoperated cases 5 died. Children and young adults are the best subjects for operation. Cases of bilateral suppuration are unsuitable. Lilienthal (Ann. of Surg., Mar., 1922).

A **rest regimen** as for active tuberculosis recommended. In acute abscess cases, 2 to 4 months' rest was required; in long-standing chronic cases, from 4 to 7 months. Other useful methods are **operation, pneumothorax, irrigation, heliotherapy, postural drainage, and vaccines**. J. S. Pritchard (Jour. Amer. Med. Assoc., Dec. 30, 1922).

Bronchoscopy is of great assistance in obscure cases and has often reversed clinical diagnoses, *e.g.*, from tuberculous to non-tuberculous suppuration, or from abscess to bronchiectasis. In all non-tuberculous, non-malignant, not hopeless cases of lung suppuration, **peroral bronchoscopic drainage** is worthy of first consideration. Chevalier Jackson (Trans. Amer. Acad. of Ophth. and Oto-Laryng., 1923).

Results in 35 cases showed that **artificial pneumothorax**, properly used, is the most successful method for acute lung abscess. It is accompanied by no shock, little pain, and complete absorption of the abscess takes place within a few weeks. The writer would advocate strongly the use of this method first in every case. If it is not successful, resort can be had to bronchoscopic or surgical methods. Tewksbury (Ann. of Clin. Med., Oct., 1925).

When occurring as sequel of pneumonia with free expectoration, an expectant plan of treatment is best, unless the process becomes progressive, in which case **surgical measures** are

imperative. In 25 cases of acute abscess following pneumonia reported by Eisendrath 24 patients recovered and 1 improved; in his chronic cases the results were less favorable.

The measures recommended under FETID BRONCHITIS (*q. v.*) are all indicated here.

PULMONARY HEMORRHAGE.

Pulmonary hemorrhage, or bleeding within the lungs, may be caused by various disorders and injuries, and erosion or rupture of the walls of the pulmonary vessels, large or small. It may be most conveniently divided into two forms: *bronchopulmonary* (bronchorrhagia), in which the blood flows into the bronchi and is eliminated through the mouth—constituting hemoptysis, and *pulmonary apoplexy* (pneumorrhagia), in which the blood accumulates in the pulmonary parenchyma, or the lung-tissue and the air-cells.

Bronchopulmonary Hemorrhage.—Although this form of hemorrhage is one of the prominent symptoms of pulmonary tuberculosis, it is important to realize that the latter affection is by no means the only one in which hemoptysis may occur. It is a comparatively frequent accompaniment of cardiac disorders; diseases of the nasal cavities, pharynx, larynx, and trachea; aneurism; menstruation; arthritism; purpura hemorrhagica; hemophilia; the *Distomum pulmonale* and other disorders, and severe injuries of the thorax.

SYMPTOMS AND DIAGNOSIS.

—In rare cases the quantity of blood is so great that the flow occurs from the nose and the mouth simultaneously. In quantity the hemorrhage usually varies from 1 ounce (30 c.c.) to a pint (500 c.c.). Fatal hemor-

rhage may occur in a cavity without hemoptysis (Osler). Again, it may be swallowed as rapidly as it reaches the laryngeal aperture, enter the stomach, and be regurgitated. But, in the majority of cases, the flow is not great; the patient first experiences a warm, salty taste, then ejects more or less great quantities of bright-red, frothy blood. It may be brought up with a cough, or suddenly fill the mouth and be expectorated. Small quantities may be brought up from time to time and merely permeate the saliva with films or streaks. The first hemoptysis may prove to be the last; it may recur a few hours later or the next day. When repeated hemorrhages occur, the last sputa assume a dark aspect; this represents blood which has sojourned in the bronchi, and usually indicates an early cessation. A small hemorrhage causes alarm in the patient, with mental agitation, dyspnea, a sensation of heat in the chest, cardiac palpitation, and other nervous symptoms; large hemorrhages give rise to the symptoms of shock and those of symptomatic anemia and unconsciousness not infrequently occur.

If it is found that the spitting of blood occurred only after a prolonged bout of coughing, it is likely that the blood came from the nasopharynx or pharynx. If it occurred spontaneously, and if the first thing the patient was aware of was the presence of blood or a salty taste in the mouth, and if the hemoptysis went on for some hours or days and was not small in amount, tuberculosis of the lungs is the probable cause. If the patient is a child, care should be taken to exclude the presence of enlarged tonsils and adenoids, on the one hand, and of chronic bronchitis, on the other, before making the diagnosis of pulmonary tuberculosis. The

other physical signs present will be of the greatest service in diagnosis, and in doubtful cases particular care should be given to the examination of the nose, nasopharynx, lungs, and heart. Not less important is the examination of the sputum for tubercle bacilli and for fragments of elastic tissue from the lungs, in any doubtful case. Should the examination prove negative, it must be repeated several times before the exclusion of pulmonary tuberculosis is justifiable. If the patient complains of spitting up streaks of blood every morning when he gets up, and at no other time, then he probably has chronic rhinitis if an adult, enlarged tonsils and adenoids if a child.

The amount of blood expectorated is of some, though relatively limited, value from a diagnostic point of view. A copious hemoptysis from several fluidounces to several pints suggests tuberculosis, aneurism, or bronchiectasis; a moderate hemoptysis, tuberculosis, or mitral disease; from the spitting up of streaks of blood no diagnostic deduction can be drawn. (*N. Y. Med. Jour.*, from *Pract.*, Nov., 1911.)

Blood from the pulmonary tract is usually thoroughly mixed with the sputum and is bright red and foamy. When this is swallowed and then vomited, fresh foamy blood generally comes with it, showing that it is not true hematemesis. The patient often imagines the amount of blood lost as far above what it really is; he must be tranquilized at all costs, and all persons that cannot be relied on must be excluded from the room, whether hemorrhage was slight or severe. The family can be reassured that with tuberculosis hemoptysis is rarely fatal. Grober (*Deut. med. Woch.*, Feb. 26, 1914).

A moderately large or a severe hemoptysis, other gross causes being excluded, suggests a tuberculous, actively evolutive tuberculous lesion, the exceptions being cases of rapidly healing or abortive tuberculosis. Glover (*Practitioner*, Aug., 1918).

Besides pulmonary tuberculosis (see TUBERCULOSIS), of which pulmonary hemorrhage is one of the prominent earlier symptoms, and the diseases—such as purpura hemorrhagica, hemophilia, scurvy, malignant infectious diseases, hepatic cirrhosis, etc.—that are often attended by this symptom, hemoptysis may occur in the following disorders:—

Cardiac Disorders.—Hemoptysis frequently occurs when valvular disorders involving stenosis are present, and especially when the mitral and aortic valves are diseased. Besides the general symptoms of the cardiac affection, the character of the blood assists in establishing the diagnosis. Instead of being bright red and frothy, as in tuberculosis, it is, as a rule, dark and more or less mixed with mucus. It does not present itself in the mouth in sudden jets, but usually comes up as would mucopurulent sputa. Again, the hemoptysis continues several weeks, sometimes without causing untoward symptoms.

Menstruation.—Hemoptysis sometimes replaces menstruation in women (vicarious menstruation). The hemorrhages are then periodical, or they may be observed as a sequel to the menopause and occur repeatedly; also at regular intervals. All such cases should be watched, debility and vulnerability of the pulmonary structures being at times either concomitant or resulting conditions under such circumstances. Periodical hemoptysis is occasionally observed after removal of the ovaries. In hysterical hemoptysis the hemorrhage is slight and pus-cells are absent, but there is present a considerable amount of squamous epithelia, leptothrix, and food remnants (Strümpell).

Nasopharyngeal Disorders.—These are frequently attended by slight hemorrhage; as a rule, the blood is brownish and the symptoms of chronic nasopharyngitis or other local disorders may be present. Tumors, especially fibroma and sarcoma of the nose and nasopharynx, may give rise to copious hemoptysis; but recurrent epistaxis often attracts attention to the seat of the disease. In epistaxis the blood may enter the nasopharynx, cause cough, and be expelled, as in hemoptysis. In a case of my own, copious recurrent hemorrhage was traced to an ulcer in the pharyngeal vault, which proved to be tuberculous. Varices of the pharynx and lingual tonsil occasionally rupture, and may give rise to a copious flow of blood.

Laryngeal Disorders.—In cancer and sarcoma of the larynx, angular foreign bodies in the laryngeal cavity, rupture of a superficial vessel, especially after straining or vomiting, and laryngitis sicca, hemoptysis is of occasional occurrence. Here, also, the blood usually comes up as would ordinary mucus, but it is often unmixed and distinctly arterial. When due to the presence of tumors, shreds of detritus are often coughed up simultaneously.

Aneurism.—This is not an uncommon cause of hemoptysis, through the pressure exerted by the aneurismal mass upon the pulmonary structures and erosions of their tissues. The trachea is frequently pressed upon in this manner by aortic and innominate aneurisms and the bleeding spot may occasionally be located with the aid of the laryngoscope. Aneurisms of the pulmonary artery, when they rupture, suddenly fill the lung with blood, causing death.

Aortic aneurisms may also rupture into the bronchial tract. The blood is ejected in mouthfuls and the secondary manifestations—pallor, unconsciousness, etc.—rapidly follow.

Vascular Fibrosis.—In atheromatous degeneration, especially in elderly persons, the pulmonary capillaries and small vessels of the bronchi sometimes yield, giving rise to a more or less copious flow. This form of hemoptysis was called by Sir Andrew Clark “arthritic hemoptysis.” It has occasionally proved fatal; but, as a rule, it constitutes a benign form of hemoptysis.

Case of fatal pulmonary hemorrhage due to *periarteritis nodosa*. The patient was a man of 23 years. The left pleural cavity was found to contain a large amount of blood, and the left lower lobe was dark red, airless, and studded with hemorrhagic infarcts. The histologic study demonstrated all the small and medium-sized branches of the pulmonary artery in the lobe mentioned to be diseased, with necrotic media, adventitia infiltrated with leucocytes, and sometimes endarteritis. Sternberg (Wien. klin. Woch., June 25, 1925).

Emphysema.—This affection is sometimes attended by hemorrhage. The blood, unless the quantity be great, is not brought up as it leaves the ruptured capillaries; it usually sojourns some time in dilated alveoli, and is coughed up in thick masses, which sometimes assume the shape of the smaller tubes and are voided as casts.

Thoracic Injuries.—Blows upon the chest, besides penetrating and crushing wounds, often cause hemoptysis, which may continue several days. (See CHEST, INJURIES OF.)

Unassignable Causes.—Finally, recurrent hemoptysis sometimes occurs

without apparent cause, notwithstanding careful search, and the subject, after a period of great anxiety, does not find his health to have been impaired, and lives many years—sometimes as a standing negation of an injudicious and hasty diagnosis. Now that microscopic examination of the sputum alone forms the basis of the decision when tuberculosis is suspected, such errors are not as frequent. Cases of this kind, however, should be watched, and, if the patient be weakly and anemic, measures tending to improve the general tone should be instituted and continued long enough to restore the patient to perfect health.

The frequency of hemoptysis in Asiatic troops and workmen from Indo-China and other Oriental countries was noted by the writers. They recall, however, that bronchitis in an Asiatic that drags along and is accompanied by blood in the sputum, calls for hospital care and strict disinfection of the sputum, as it is liable to contain the eggs of the *Paragonimus westermani* or *Distoma ringeri*. They insist that the discovery of distomatosis of the lungs is a warning to deport the patient if his condition permits. These are the only means to prevent development of foci of endemic distomatosis. Salomon and Neveu (Revue de Méd., Nov.-Dec., 1916).

Pulmonary Apoplexy (Pneumorrhagia).—This consists in extravasation of blood into the air-cells and interstitial pulmonary tissue, as a result of aneurismal rupture, penetrating wounds, ulceration involving a large vessel, septicopyemia, cerebral disease, and other conditions in which the pulmonary parenchyma is torn. In circumscribed pneumorrhagia the blood may be effused into the air-cells and the interstitial tissue, without laceration of the pulmonary

parenchyma, as in cases of pulmonary embolism or hemorrhagic infarction.

Diffuse pulmonary apoplexy arises from a rupture of a thoracic aneurism that has become adherent to the lung-surface. Its more usual course is traumatism, particularly penetrating wounds. It is more common in adult males.

As here understood, pulmonary apoplexy only applies to rarely observed cases in which the organ is overwhelmed with blood, which gushes out of the mouth in great volume. Intense dyspnea, collapse, and death follow in quick succession. In some cases the hemorrhage is, so to say, localized, and the hemoptysis is not severe. Soon, however, an abscess and at times gangrene appear, and the patient succumbs from septicopyemia.

TREATMENT OF PULMONARY HEMORRHAGE.—The treatment of pulmonary hemorrhage not only varies with the cause, but therapeutic measures addressed to the cardiovascular system at large are also necessary. Examination of the upper respiratory tract, the nasopharynx, the pharynx, the larynx, the trachea, the base of the tongue, etc., may reveal a bleeding spot and call for the local application of **styptics**; besides this, however, measures tending to reduce the vigor of cardiac action—**rest**, etc.—must be resorted to. A third class of therapeutic indications are those calculated to prevent the recurrence of the hemorrhages.

If the hemorrhage is a copious one, the patient should at once be placed in a **reclining position**, his **head** being turned to **one side** to enable him to clear his mouth as fast as it is filled.

Whatever be the cause of the bleeding, it cannot be clearly established while it lasts; general measures are therefore alone indicated for the time being. Several remedies at present commonly employed are more pernicious than helpful, particularly ergot and the ice poultice. Ergot increases vascular tension; the ice poultice contracts the peripheral vessels and causes engorgement of the deeper vessels.

Probably the most effective agents are **morphine** and **atropine**, $\frac{1}{4}$ grain of the former and $\frac{1}{100}$ grain of the latter, given together hypodermically. At the same time, a large handkerchief, napkin, towel, or **bandage** should be **tightly wound around each extremity**, as near the trunk as possible, to momentarily arrest the return of the venous blood to the thoracic organs. This procedure, if properly carried out, at once reduces the pulmonary engorgement and usually arrests the flow unless it is overwhelming. **Nitrite of amyl** is another remedy which acts promptly. Fish reports excellent results from the **inhalation of chloroform** in 19 cases. He uses from $\frac{1}{2}$ to 1 fluidram (2 to 4 c.c.) at once; later, the inhalation of 15 or 20 drops every hour is used for several days. Foxwell advises **venesection** when venous congestion is present, combined with measures that confine the blood to the systemic circulation (**nutritious food**, large doses of the **nitrites**, **hot foot baths**, **leeches to the anus**, and **ligatures to the thighs and arms**). Anders has found **dry cupping** over the chest of great service in cases dependent upon congestion, combined with the free use of **iced drinks** and the eating of **ice**. Wilkinson asserts that **tuber-**

culin has prophylactic and curative action. When these agents cannot be obtained, a tablespoonful of **salt** dissolved in a tumblerful of water generally arrests the flow when the bandages are also applied as stated.

The writer obtained excellent results from the use of **amyl nitrite** in cases of hemorrhage due to bullet wounds of the lungs. He used 5-minim (0.3 c.c.) pearls by inhalation. When it is desired to maintain the effect, the writer administers **nitroglycerin** and **sodium nitrite** in small and oft-repeated doses. Sweet (Military Surgeon; Monthly Cyclop., May, 1908).

A combination of **epinephrin**, **calcium chloride**, and **opium** is almost specific in hemoptysis; other remedies have been overrated. Locally, **ice** and **mustard** are valuable. If these fail, **ipercac** and **tartar emetic** may stop the flow. Gilbert (Paris méd., July 13, 1912).

The subcutaneous injection of 40 c.c. ($1\frac{1}{2}$ fluidounces) of **sterile gelatin solution** causes a twenty-four hours' rise in viscosity of the blood by 1.4 of original value, and reduces tendency to hemoptysis. Cmunt (Med. Klinik, Aug. 25, 1912).

Gratifying results from **intravenous saline infusion** in 50 cases; 5 c.c. (80 minims) of a 10 or 15 per cent. **solution of sodium chloride** used. Causes no pain and is entirely innocuous. Müller (Beiträge z. Klinik der Tuberkulose, Bd. xxviii, Nu. 1, 1913).

If the blood-pressure is less than 110 the writer gives an intravenous injection of 0.5 Gm. ($7\frac{1}{2}$ grains) of **ergotin** dissolved in 1 c.c. (16 minims) of distilled water. If the blood-pressure is higher than 110 there is injected in addition 0.001 Gm. ($\frac{1}{4}$ grain) of **morphine hydrochloride**. A few minutes after the administration the cough and hemoptysis cease. Garmagnano (Riforma Medica; Charlotte Med. Jour., Nov., 1913).

Camphorated oil is of great value. Volland has also been very success-

ful with subcutaneous injections of from 25 to 30 Gm. ($6\frac{1}{4}$ drams to 1 ounce) of a 10 per cent. camphorated oil. But the writer has found it preferable to give moderate doses of the 20 per cent. oil. Zehner (Zeit. f. Tuberk., Aug., 1920).

A 500 c.c. (1 pint) **enema of milk** is promptly effective where the usual remedies fail. The author gives 250 c.c. at night, after a cleansing enema, in all patients with the least sign of hemorrhage, until the red tinge of the sputum has disappeared. Geers (Nederl. Tijdschr. v. Geneesk., Apr. 29, 1922).

Slow intravenous injection of large doses of **sodium citrate**, up to 5 Gm. (75 grains), successfully used in arresting hemorrhages due to tuberculosis, gastric ulcer, typhoid fever, and other conditions without diminution or disease of the blood platelets. N. Rosenthal and G. Bachr (Arch. of Int. Med., May, 1924).

Throughout, the patient should be kept absolutely **quiet**. He should be informed that his hemorrhage is not likely to prove lethal, and also enjoined against unnecessary coughing.

Excellent results have been reported in hemoptysis from hypodermic injections of $\frac{2}{3}$ to 1 grain (0.04 to 0.06 Gm.) of **emetine hydrochloride**, and from hypodermic or intravenous administration of liquid **pituitary extract**, 8 minims (0.5 c.c.) at a dose.

Artificial pneumothorax has proven very useful in uncontrollable hemoptysis.

In 10 cases, immediately following injection of **pituitrin** intravenously, there was complete arrest of the hemorrhage, and the physical signs over the area from which the blood was supposed to come were materially modified. Rist (Bull. Soc. méd. des hôp. de Paris, Apr. 24, 1913).

Without nauseating or reducing the blood-pressure appreciably, the tendency to hemorrhage is arrested almost at once by injection of 0.04 to 0.00 Gm. ($\frac{1}{2}$ to 1 grain) of **emetine hydro-**

chloride. This occurs apparently irrespective of the cause. Aubert, Bouyer, and Chauffard (Bull. de l'Acad. de méd., Jan. 20, 1914).

Atropine sulphate used hypodermically, $\frac{1}{30}$ grain (0.002 Gm.), repeated once in 6 hours if necessary. Landis (Ther. Gaz., Mar., 1922).

The writer prefers **morphine**, and gives second place to **limitation of fluids** and **sodium chloride**, 1 to 2 drams (4 to 8 Gm.) every 3 hours, with **sodium bromide**, 20 to 30 grains (1.3 to 2 Gm.). **Artificial pneumothorax** should always be considered in persistent blood spitting (which depresses the patient) and in severe hemorrhage at any stage of the disease. The necessity of knowing which is the bleeding side is a limitation in its use, but complete compression is not always necessary, brilliant results being often achieved even where partial adhesion restricts the injection. W. G. Turnbull (Ther. Gaz., Mar., 1922).

Strapping the half of the chest with adhesive plaster strips, forming a stiff cuirass, recommended. Viton (Semana méd., Feb. 12, 1925).

Grünbaum has advised 2 minims (0.12 c.c.) of **tincture of aconite** (B. P.) every hour until the pulse is reduced below 65 or becomes irregular, or the blood-pressure falls below 90 mm. of mercury.

After the hemorrhage has ceased, the patient should remain where he is an hour or so, then be carried on a litter to a cool room. He should not be allowed to speak. Fainting tends to assist clotting and the patient, as a rule, recovers his senses within a short time. The bandages should be removed gradually, fifteen minutes being allowed between the successive operations, so as to avoid a sudden tension on the pulmonary arteries. **Aconite** or **veratrum viride** may then be used.

The diet allowed should be light. Much liquid of any kind and hot

beverages tend to bring on a recurrence of the flow. To assist in preventing this, the formation of a clot should be encouraged; this is best accomplished by **calcium chloride**, 10 to 15 grains (0.6 to 1 Gm.) every two hours in glycerin, or **calcium lactate**, 30 grains (2 Gm.) in solution, three times a day. **Saline purgatives** are valuable to reduce vascular tension, but they should not be utilized when the patient has been greatly weakened by the hemorrhages if other measures are effective. **Magnesium sulphate** in the dose of 1 to 2 ounces (30 to 60 Gm.) is frequently used.

The tuberculous who spit a little blood morning or night, and none the rest of the day, almost always have some circulatory trouble. Let them **drink water** and live on a **vegetarian diet**, and 9 out of 10 will lose the last trace of blood in forty-eight hours. Forced feeding is injurious for the tuberculous with a cardiac taint; they should drink as little as possible with their meals, to prevent distention of the stomach and its injurious action on the heart. When the patients once realize the benefit from these rules, they apply them habitually, eating little meat, masticating with special care, and drinking water only between meals. Sabourin (Arch. gén. de méd., Aug., 1912).

The hemoptysis observed in *elderly persons*, and due to vascular disorders, is, according to Sir Andrew Clark, aggravated or maintained by the frequent administration of large doses of strong astringents, by the application of ice-bags to the chest, and by indulgence in liquids to allay the thirst created by the astringent. The treatment found most successful by him in these cases is **diet; quiet, restricted use of liquids, stilling of the cough, calomel, salines, alkalies with iodide of potassium**, and frequently

renewed **counterirritation**. (See also TUBERCULOSIS.)

In all cases the cessation of hemorrhage should not interrupt treatment, as in many cases there is a tendency to recurrence. For small and repeated hemorrhages, **turpentine** and **aromatic sulphuric acid** are indicated. The use of **stimulating food, tobacco, alcoholics**, and all **physical and mental strain** should be **forbidden**. Bronchial irritation should be avoided, and attacks of bronchitis, though mild, should be carefully treated. An **inland climate** is advised, with **moderate exercise** and **abundant nutritious food**.

PULMONARY EMBOLISM (HEMORRHAGIC INFARCTION; EMBOLISM OF THE LUNG).

This consists of a mechanical obstruction of one or more pulmonary arteries by an embolus or thrombus.

SYMPTOMS.—While a diminutive infarction may pass unnoticed, complete occlusion of a large pulmonary artery may occasion instant death. Symptoms arise when the embolus does not completely fill the lumen of the artery involved, or when the latter is not of sufficient size to completely disturb the pulmonary circulation, even though the vessel be completely occluded. Under these circumstances, dyspnea is experienced. It gradually increases in severity, and may be preceded by unconsciousness and convulsions. The patient gasps for breath and indicates, by his frantic efforts to inhale, the intensity of his suffering. The pulse becomes weak and thready; the skin is cold and clammy and is covered with sweat. Severe localized pleuritic pain and a hard and harassing cough are usually present, and the patient

expectorates masses of bloody or dark gelatinous mucus. This reveals, upon microscopic examination, peculiar large lymph-cells resembling alveolar cells and containing blood-corpuscles. These giant cells are thought to transform the blood-corpuscles into pigment-matter. They are seen especially in cases of heart disease, and are known as the "cells of heart-failure" (Whittaker). As the case progresses, local suppuration with metastatic abscesses occurs, and all the evidences of pyemia may appear. Dissolution of the thrombus may take place and the abscesses may undergo resolution, but, as a rule, the prognosis is serious.

Tragic deaths from pulmonary embolism, both after operations and confinements, are due principally to a hyperfibrinous blood. All patients should drink water freely. He also urges that the position of the patients be changed frequently and that they move their limbs freely as soon as possible, and that they sit on a chamber in bed to pass water and move the bowels. Lying on the back for ten days, with the blood getting more clottable daily is a very good way to bring about thrombosis and death by embolism when the patient begins to move about. Pulmonary embolism is rare, only 47 deaths having occurred from it at the Mayo Clinic in 63,000 operations. A. L. Smith (Brit. Med. Jour., June 8, 1918).

DIAGNOSIS.—When associated with the symptoms enumerated,—dyspnea, syncope, bloody expectoration, etc.,—the physical signs assist in establishing the diagnosis. But they are only clearly obtained when the lesion is not too deeply seated. A localized consolidation giving rise to dullness under percussion, bronchial respiration, increased fremitus, moist râles, and a friction-sound,

when the tension is near the pleura, represent the only signs which may be attributed to the embolus, all others being due to conditions developed secondarily.

ETIOLOGY AND PATHOLOGY.

—Pulmonary embolism is due to stasis, in the majority of cases, the primary factor being a pulmonary or cardiac affection. The infarct generally consists of a wedge-shaped mass of leucocytes and red corpuscles with its base usually at the pleura, which soon becomes dull looking and covered with fibrin. It is usually firm, airless, and black or brownish and varies in size from that of a cherry to that of an entire lobe, since in some cases the entire vascular supply of a lobe is involved. Its envelope is formed of a thin film of fibrin. Hemorrhagic infarctions often develop near the pleura and at the back of the lower lobe. They may be single or multiple and may involve the greater part of the lobe, though usually they are about the size of a walnut. Their seat of election is at the back of the lower lobe. Leucocytes and red blood-corpuscles are present in the air-cells and in the alveolar septa. Collateral congestion and edema are usually present.

Among 63 cases of post-operative pulmonary complications, the writers found 32 of pulmonary infarction and 2 of pulmonary embolism. The infrequency of lobar pneumonia in this series agreed with the more accurate recent studies of this disease as a post-operative lesion due to embolism rather than infection. Of the 32 cases of pulmonary infarction, all but 7 were laparotomies. The onset occurred from the 2d day to the 3d week, usually with sudden pain on respiration, followed by expectoration, often blood-tinged, the symptoms being preceded

beverages tend to bring on a recurrence of the flow. To assist in preventing this, the formation of a clot should be encouraged; this is best accomplished by **calcium chloride**, 10 to 15 grains (0.6 to 1 Gm.) every two hours in glycerin, or **calcium lactate**, 30 grains (2 Gm.) in solution, three times a day. **Saline purgatives** are valuable to reduce vascular tension, but they should not be utilized when the patient has been greatly weakened by the hemorrhages if other measures are effective. **Magnesium sulphate** in the dose of 1 to 2 ounces (30 to 60 Gm.) is frequently used.

The tuberculous who spit a little blood morning or night, and none the rest of the day, almost always have some circulatory trouble. Let them **drink water** and live on a **vegetarian diet**, and 9 out of 10 will lose the last trace of blood in forty-eight hours. Forced feeding is injurious for the tuberculous with a cardiac taint; they should drink as little as possible with their meals, to prevent distention of the stomach and its injurious action on the heart. When the patients once realize the benefit from these rules, they apply them habitually, eating little meat, masticating with special care, and drinking water only between meals. Sabourin (Arch. gén. de méd., Aug., 1912).

The hemoptysis observed in *elderly persons*, and due to vascular disorders, is, according to Sir Andrew Clark, aggravated or maintained by the frequent administration of large doses of strong astringents, by the application of ice-bags to the chest, and by indulgence in liquids to allay the thirst created by the astringent. The treatment found most successful by him in these cases is **diet; quiet, restricted use of liquids, stilling of the cough, calomel, salines, alkalis with iodide of potassium**, and frequently

renewed **counterirritation**. (See also TUBERCULOSIS.)

In all cases the cessation of hemorrhage should not interrupt treatment, as in many cases there is a tendency to recurrence. For small and repeated hemorrhages, **turpentine** and **aromatic sulphuric acid** are indicated. The use of **stimulating food, tobacco, alcoholics**, and all **physical and mental strain** should be **forbidden**. Bronchial irritation should be avoided, and attacks of bronchitis, though mild, should be carefully treated. An **inland climate** is advised, with **moderate exercise** and **abundant nutritious food**.

PULMONARY EMBOLISM (HEMORRHAGIC INFARCTION; EMBOLISM OF THE LUNG).

This consists of a mechanical obstruction of one or more pulmonary arteries by an embolus or thrombus.

SYMPTOMS.—While a diminutive infarction may pass unnoticed, complete occlusion of a large pulmonary artery may occasion instant death. Symptoms arise when the embolus does not completely fill the lumen of the artery involved, or when the latter is not of sufficient size to completely disturb the pulmonary circulation, even though the vessel be completely occluded. Under these circumstances, dyspnea is experienced. It gradually increases in severity, and may be preceded by unconsciousness and convulsions. The patient gasps for breath and indicates, by his frantic efforts to inhale, the intensity of his suffering. The pulse becomes weak and thready; the skin is cold and clammy and is covered with sweat. Severe localized pleuritic pain and a hard and harassing cough are usually present, and the patient

expectorates masses of bloody or dark gelatinous mucus. This reveals, upon microscopic examination, peculiar large lymph-cells resembling alveolar cells and containing blood-corpuscles. These giant cells are thought to transform the blood-corpuscles into pigment-matter. They are seen especially in cases of heart disease, and are known as the "cells of heart-failure" (Whittaker). As the case progresses, local suppuration with metastatic abscesses occurs, and all the evidences of pyemia may appear. Dissolution of the thrombus may take place and the abscesses may undergo resolution, but, as a rule, the prognosis is serious.

Tragic deaths from pulmonary embolism, both after operations and confinements, are due principally to a hyperfibrinous blood. All patients should drink water freely. He also urges that the position of the patients be changed frequently and that they move their limbs freely as soon as possible, and that they sit on a chamber in bed to pass water and move the bowels. Lying on the back for ten days, with the blood getting more clottable daily is a very good way to bring about thrombosis and death by embolism when the patient begins to move about. Pulmonary embolism is rare, only 47 deaths having occurred from it at the Mayo Clinic in 63,000 operations. A. L. Smith (Brit. Med. Jour., June 8, 1918).

DIAGNOSIS.—When associated with the symptoms enumerated,—dyspnea, syncope, bloody expectoration, etc.,—the physical signs assist in establishing the diagnosis. But they are only clearly obtained when the lesion is not too deeply seated. A localized consolidation giving rise to dullness under percussion, bronchial respiration, increased fremitus, moist râles, and a friction-sound,

when the tension is near the pleura, represent the only signs which may be attributed to the embolus, all others being due to conditions developed secondarily.

ETIOLOGY AND PATHOLOGY.

—Pulmonary embolism is due to stasis, in the majority of cases, the primary factor being a pulmonary or cardiac affection. The infarct generally consists of a wedge-shaped mass of leucocytes and red corpuscles with its base usually at the pleura, which soon becomes dull looking and covered with fibrin. It is usually firm, airless, and black or brownish and varies in size from that of a cherry to that of an entire lobe, since in some cases the entire vascular supply of a lobe is involved. Its envelope is formed of a thin film of fibrin. Hemorrhagic infarctions often develop near the pleura and at the back of the lower lobe. They may be single or multiple and may involve the greater part of the lobe, though usually they are about the size of a walnut. Their seat of election is at the back of the lower lobe. Leucocytes and red blood-corpuscles are present in the air-cells and in the alveolar septa. Collateral congestion and edema are usually present.

Among 63 cases of post-operative pulmonary complications, the writers found 32 of pulmonary infarction and 2 of pulmonary embolism. The infrequency of lobar pneumonia in this series agreed with the more accurate recent studies of this disease as a post-operative lesion due to embolism rather than infection. Of the 32 cases of pulmonary infarction, all but 7 were laparotomies. The onset occurred from the 2d day to the 3d week, usually with sudden pain on respiration, followed by expectoration, often blood-tinged, the symptoms being preceded

in about $\frac{1}{2}$ the cases by rise in pulse, temperature and respiration. The friction rub may be the most distinct sign, but only when the infarct reaches the periphery of a lobe. Immediate auscultation reveals one or more small areas filled with fine râles and impairment of breath sounds. A promptly taken roentgenogram invariably demonstrates one or more small areas of consolidation. Adjustment to normal blood distribution is usually complete in 6 or 7 days. This complication occurs frequently even with local anesthesia. Cutler and Hunt (Arch. of Int. Med., Apr., 1922).

Frequent sources of emboli lie in thrombosed veins of the uterus following childbirth, the femoral, pelvic, hemorrhoidal and prostatic veins. After appendicitis, pulmonary embolism is commonest when the diseased appendix is situated postcecally and high up. Embolism may also result from venous thrombosis attending typhoid fever. Pleurisy with effusion is another possible source.

In a collection of 114 cases of pulmonary embolism the average age was 52 years. The site of the primary thrombus was discovered in 42 per cent. of cases. It occurs in veins in which there is marked stasis. Sepsis is probably only a contributory cause, promoting stasis by lowering vitality. Lindsay (Lancet, Feb. 14, 1925).

After laparotomies or operations for hernia or on the bladder or rectum, the source of the embolus is often in the hypogastric and femoral veins, and at times in the saphenous or spermatic vein. In one-half the cases the embolism occurs 4 to 14 days after the operation (Petren).

Data from various clinics revealed an incidence of something less than 1 fatal case in 1000 operations. In the Adelaide Hospital, 1 to 3 per cent. of operative deaths are attributable to pulmonary embolism. Survival longer

than 10 minutes implies a fair chance of recovery if no secondary pneumonia follows. The cause of death is the sudden strain on the right heart incident to the obstruction to the flow of blood from it. Cutting off of the breathing surface is of minor moment. Lockhart-Mummery (Brit. Med. Jour., Nov. 8, 1924).

Fat embolism may follow fractures, and metastases from neoplasms may likewise be the source of embolism and infarction.

Movements calling for strong contraction of the abdominal muscles are regarded as being the most likely to cause embolic complication.

The fact that pulmonary embolism does not occur in children, nor in operations on the upper limbs, seems to support the view that slow venous circulation is an important factor.

TREATMENT.—The patient's strength should be sustained and his position so adjusted as to facilitate respiration; this is usually best accomplished by **elevating the upper part of the body**. In addition to **absolute rest** and relief of the distressing symptoms, treatment should be directed against the causative disease. Dyspnea and pain may be relieved by the use of **morphine** and **atropine**. Gessner recommends hypodermic injections of **ether** or **morphine**. **Amyl nitrite** is recommended, to relieve the strain on the right heart.

To overcome dyspnea and the tendency to syncope, injections of **camphor** and **ether** should be given:—

R *Camphoræ* ʒv (20 Gm.).

Ætheris fʒviiss (25 c.c.).

Olei olivæ sterilisati q.s. ad fʒiiiiss (100 c.c.).

M. Sig. Give hourly injections of 30 minims (2 c.c.).

One or two liters of **oxygen** should simultaneously be injected under the

skin, and their effect kept up with repeated oxygen inhalations.

Next, **dry cups** should be applied to the **chest**, and, if hemoptysis is not marked, from 4 to 6 of the **areas** may be **scarified** on the side that is subjectively painful. **Venesection** is indicated only where there are evidences of pulmonary edema. Where pain is not relieved by the cupping an injection of **morphine** should be given, to be immediately followed by one of **ether** or **sparteine**.

Cough, which is generally marked, should be assiduously combated, as it increases dyspnea and favors hemoptysis:—

℞ *Extracti opii* .. gr. $\frac{1}{6}$ (0.01 Gm.).
Extracti hyoscy-
ami,
Extracti stra-
moniiãã gr. $\frac{1}{42}$ (0.005 Gm.).

Fiat pilula no. j.

Sig.: One pill every two or three hours.

To prevent, in so far as is possible, suppuration or gangrenous degeneration of the infarct, a tablespoonful of the following mixture may be placed in a vessel containing water that is kept boiling:—

℞ *Olei thymi,*
Olei eucalypti,
*Olei terebinthinæ.*ãã f̄iiss (10 c.c.).
Tincturæ benzoini. f̄ij (30 c.c.).
Alcoholis ..q. s. ad f̄viij (250 c.c.).

Misce.

Another available procedure is to pass the oxygen that is being inhaled by the patient through the following combination, contained in a flask:—

℞ *Thymolis* gr. xlv (3 Gm.).
Eucalyptolis m̄lxxv (5 c.c.).
Phenolis gr. lxxv (5 Gm.).
Alcoholis absoluti. f̄iiv (125 c.c.).
Aquæq. s. ad Oij (1000 c.c.).

Misce.

In exceptional cases surgical intervention—**Trendelenburg's operation**—can be undertaken. Oppenheim (N. Y. Med. Jour., from Progrès méd., Feb. 15, 1913).

If the patient survives the first hour, his pain and distress must be relieved with **morphine**. This is particularly useful in case of embolism in the smaller branches of the pulmonary artery, which often is accompanied by intense pain in the pleura. This can be combated with **ice** or **mustard**, **cold-water bandaging**, or **wet cupping**. Grober (Deut. med. Woch., Feb. 19, 1914).

Surgical treatment has been attempted in a few cases by Trendelenburg and others, with partial success.

One is justified in attempting to remove the obstruction embolus, as Trendelenburg's and Siever's patients lived afterward for thirty-seven and fifteen hours and Kruger's for over five days, succumbing finally to purulent pleuritis. But it is useless to attempt operative removal of the embolus if there is heart disease or wasting sickness. Schumacher (Archiv f. klin. Chir., Bd. ci, Nu. 3, 1913).

PULMONARY EDEMA.

DEFINITION.—Edema of the lungs is due to the escape of serum through the vascular walls into the alveolar wall and interstitial tissue. It is a secondary condition, is generally associated with pulmonary congestion, and is usually bilateral.

SYMPTOMS.—Edema appears and progresses more or less insidiously, the dyspnea resulting from reduced respiration being marked in proportion. The respiration at first becomes hurried; a feeling of suffocation is experienced, accompanied by considerable anxiety and great muscular effort to facilitate the respiratory act. Cyanosis soon appears if the effusion involves much interstitial tissue, particularly when collateral edema exists, and intense suffering is sometimes witnessed. The infiltration is usually bilateral and ascends from the lower lobes.

The sputum may not be increased at first, but, as soon as the quantity of serum in the alveoli becomes great, it becomes very abundant and frothy and is expectorated with great difficulty. In some cases it is thin and watery; in others it is sufficiently viscid to markedly increase the dyspnea through laryngeal obstruction. A peculiarity of the sputum at this stage is that it is more or less tinged with red, due to the presence of red blood-corpuscles. It may also contain urea.

The pulse is generally rapid and feeble, the weakness increasing as the infiltration progresses. No fever is present unless due to an intercurrent or underlying affection. The extremities become cold and the patient in extreme cases dies from heart-failure and carbon dioxide poisoning.

In acute suffocative edema there is great shortness of breath, soon followed by cough and expectoration. The lungs are filled with moist râles, which persist for several days and then gradually disappear. There is generally a rise of temperature to about 100° F. and great prostration the day after the attack. Recovery is complete, even without treatment. Prompt relief is, however, often secured by giving **nitroglycerin** or a hypodermic of **morphine**. The cause of such attacks is probably related to anaphylaxis, the offending substance being, perhaps, a nitrogenous metabolic product. Prophylaxis would then consist in reducing the protein intake to a minimum and at the same time keeping the patient's physical condition above par. The attacks may also be prevented by continuous use of $\frac{1}{2}$ to $1\frac{1}{2}$ grains (0.03 to 0.1 Gm.) of powdered **digitalis** daily. L. F. Bishop (Jour. Amer. Med. Assoc., Dec. 9, 1922).

In 2 cases observed by the writer, acute pulmonary edema occurred in patients suffering from acute nephritis.

In 1 case there was no apparent cause for or warning of the attack, while in the second, the edema followed aspiration of the pleural cavity. Binns (Med. Jour. of Austral., Aug. 9, 1924).

Examination at once reveals the reduced respiratory area, through inspection, the motions of the chest being restricted; percussion shows dullness over the infiltrated regions and resonance—at times tympanitic—above; auscultation, eliciting moist mucous and submucous râles, with gurgling on inspiration and at the beginning of expiration over the site of the edema, increasing as the involved tissues are approached. The vesicular murmur is feeble or absent, or there may be bronchovesicular breathing.

With Bianchi's phonendoscope the gradual progress of the edema can generally be traced with considerable accuracy.

A recurring variety has been noted by Crummer, Riesman, and others, appearing without any apparent cause and not infrequently proving fatal. The chief symptoms are agonizing dyspnea, cyanosis, cough, expectoration of frothy, albuminous fluid, and profound prostration. Recovery from an attack is frequent and sudden.

In the writer's twenty-seven years' practice paroxysmal edema of the lungs was met with 4 times. The attack most often commences with some irritation in the throat, tickling, and a feeling of dryness, with slight cough, and the patient has a fear of some serious happening. He can not, dare not, lie down; breathing at once becomes rapid; the face looks anxious and is pale. There is generally, but not always, some cyanosis with the pallor.

The skin of the patient is cold and moist; breathing is oppressed and urgent; cough grows more dis-

treassing, and there is some expectoration of frothy, coagulable fluid, frequently blood-stained; the chest is rapidly filled with noisy râles; the pulse is small and quick; expectoration at times becomes profuse. This condition continues for, perhaps, half an hour to an hour and a half, then gradually disappears. Flemming (*Bristol Medico-Chir. Jour.*, June, 1913).

DIAGNOSIS.—The diagnosis is not difficult, owing to the comparative suddenness of the onset, the demarcation between the free and the infiltrated areas, and the absence of fever.

Bronchopneumonia.—This affection presents some points of resemblance; but the fever is marked and the physical signs are different, no clear distinction being traceable between the affected and non-affected areas. The mucous râles occur late in the course of the disease; in the edema they are present almost from the start. The expectoration is glairy and tenacious.

Hydrothorax.—This affection also presents considerable resemblance to edema, but change of position does not alter the area of dullness in edema, whereas the flow of liquid to another part of the chest causes a corresponding change in the seat of the dullness in hydrothorax.

Moist râles are not apt to be present in hydrothorax unless it is due to a concomitant disorder.

Pulmonary edema at the apex simulates tuberculosis and may be accompanied by bronchial adenopathy. Radiography serves in diagnosis. Brunon (*Presse méd.*, May 3, 1911).

In a woman of 62, attacks of suffocation and hemoptysis were substituted for acute lung edema in chronic insufficiency of the left ventricle. Gallavardin (*Médecine*, Mar., 1921).

ETIOLOGY AND PATHOLOGY.

—Edema of the lungs usually occurs as a final complication of other affections, but it may appear idiopathically after a too-hot bath, the copious ingestion of ice water, etc. It is thought to be due to one of three general causes: paresis of the vascular walls, impediment to the free circulation in a diseased organ, or disease of the vessels with increased permeability. Huchard suggests that the increased permeability of the vessel-walls is due to impairment of their nutrition and disturbance of the cardio-pulmonic innervation. This occurs in the form due to toxic and infectious diseases, when the blood has undergone more or less change in cachectic states, uremia, general septicemia, etc. Pulmonary edema, due to vasomotor relaxation from toxic states, sometimes develops rapidly. Vascular paresis appears to be the source of the infiltration in cases occurring suddenly in healthy persons. Impediment to the circulation is found in connection with acute and chronic Bright's disease, of which it is a very frequent complication as a terminal manifestation of dropsy, septicemia, pneumonia, and other infectious diseases. In the latter case the sputum is usually more deeply blood-tinged than in the form due to renal trouble. It is also met with in grave anemia, cerebral injuries, and valvular heart affections. Increased fluidity of the blood and increased tension in the pulmonary vessels are marked factors in many cases. The increased blood-pressure may be due to a failure of cardiac power, and particularly to failure of the left ventricle (Welch). Edema may occur from weakness of the right ventricle alone. It may

also occur as a result of hypostatic congestion; it is then termed "hypostatic edema."

The transudation of serum may either be local (*i.e.*, limited to an area involved in an inflammatory process [pneumonia, abscess, or pulmonary infarction] through which the vascular walls are weakened, and osmosis of the serum rendered possible) or general. In the latter type the transudation, serous or serosanguinolent, invades the tissues and alveoli, and the lung at autopsy is much heavier than the normal organ in water, but does not sink. It is boggy and pits on pressure; on section there exudes a serous or serosanguinolent (if congestion is present) fluid of low specific gravity, and containing less albumin than plasma. Edema is most frequently found at the bases of the lungs, but may be uniformly distributed throughout these organs. Hydrothorax may coexist.

Pulmonary edema has been known to follow an unduly rapid thoracentesis; the injection of saline solutions, owing to the sudden increase of blood-pressure; inhalations of amyl nitrite, and the use of potassium iodide.

The cases of acute suffocative edema of the lungs can be divided into those occurring in persons over 40 in whom some organic lesion exists, especially aortic regurgitation, and those, like the author's case, in persons without discoverable organic disease. The latter cases, he believes, are really instances of aborted pneumonia, going no further than the congestive stage. The condition is relieved by the escape of the collected serum. Consolidation is not often demonstrated. Influenza seems to favor the condition. The writer's case in a girl of 19 occurred in a district with an influenza epidemic. She had sudden difficult breathing and

feeling of suffocation, without cyanosis. Later a few râles were audible at the left base. The temperature was elevated, and there was copious blood-stained frothy sputum, followed by dullness, bronchophony and tubular breathing at the base of the left lung. In a few days all signs and symptoms disappeared. The usual treatment for these cases is immediate **venesection**. **Wet cupping** and **mustard plasters** are also useful. W. J. Tyson (*Lancet*, Oct. 21, 1922).

Case of acute edema of the lungs ending fatally in a syphilitic woman aged 55 following an intravenous injection of 0.01 Gm. ($\frac{1}{10}$ grain) of mercury cyanide. The injections were being given 3 times a week, and the patient had previously received injections of neoarsphenamin and bismuth without intolerance. The acute lung edema occurred 15 to 20 minutes after the 5th mercurial injection, with bloody diarrhea and evidences of dilatation and insufficiency of the heart. She died 2 weeks later, and the autopsy showed chronic nephritis. Acute renal insufficiency had evidently been induced by the later mercurial injections and led to dilatation of the left ventricle and pulmonary edema. Monges and Raybaud (*Marseille méd.*, July 15, 1924).

Brief contact with a wire carrying 110 volts resulted in a severe attack of edema of the lungs in a man of neuro-pathic type. Schneider (*Münch. med. Woch.*, Mar. 13, 1925).

Case of pulmonary edema lasting 1½ hours in a bride of 69 years during the first night of the honeymoon. Recovery was complete. Pel (*Ned. Tijds. v. Gen.*, June, 1925).

PROGNOSIS.—The prognosis of pulmonary edema is grave in all cases in which it occurs as a complication, its gravity depending on that of the causative affection. In the so-called "idiopathic" cases, those occurring independently of any primary disease, the chances of recovery are much greater. The edema secondary to a

general dropsy due to cardiac or renal disease often causes rapid death. Inflammatory edema following lobar pneumonia presents a particularly unfavorable prognosis.

TREATMENT.—Edema of the lungs being due in practically all cases to another disease, the treatment of the latter is the foundation of the measures to be adopted plus one very important indication: to sustain the heart by every means possible, heart-failure being the main cause of death. The condition of the kidneys must also be closely watched. **Caffeine, digitalis, and strychnine** are the mainstays as far as remedies are concerned. **Nitroglycerin** and **atropine**, particularly the latter in full doses ($\frac{1}{50}$ grain—0.0013 Gm.—repeated every hour if required), are often beneficial. When pulmonary edema occurs in children 3 minims (0.2 c.c.) of the **tincture of strophanthus**, given every three hours, will give relief.

Derivatives are of value to relieve as much as possible the vascular engorgement. In the early stages a **hot mustard foot bath** affords considerable relief, especially if coupled with the copious use of **dry cups** over the infiltrated area.

The **position** of the patient's body should be **frequently changed**, so as to prevent hypostatic congestion.

When the edema shows signs of increase or when the case from the start assumes severe symptoms, **venesection** should at once be resorted to. If the pulse is full and the heart acting vigorously, the spasm of the minute arterioles can, according to O'Donovan, be as readily relieved by **nitroglycerin** or **morphine** as by the depressing effect of the **abstraction**

of blood. If the immediate origin of the trouble is the weakened muscle of the heart, showing its feebleness by frequent, irregular, and inefficient contractions, with a small and fluttering pulse, one should give at once under the skin $\frac{1}{100}$ grain (0.0006 Gm.) of **atropine sulphate**, with $\frac{1}{50}$ grain (0.0012 Gm.) of **strychnine sulphate**. This is to be inserted just below the clavicle in order to reach the heart with the least loss of time. While this is being absorbed attention can be given to preparations for venesection, if it should prove necessary. Atropine rapidly contracts the vessels, powerfully stimulates the sympathetic system, increases the force of the heart's beat, raises arterial tension, stimulates the respiratory centers, and dries up the secretions of the skin and mucous membranes. The dose required is whatever may be sufficient to produce its physiological effect, easily gauged by watching the amount of dilatation of the pupil. It is safe to begin with $\frac{1}{200}$ grain (0.0003 Gm.), and repeat in a half-hour or at longer intervals until the system is well under its influence.

Artificial respiration will prove more prompt and effective than any medication whenever the edema and cardiac incompetence are of sudden development and due to causes likely to prove of brief duration or removable by appropriate treatment. Emerson (Arch. of Intern. Med., May, 1909).

Case in which the edema seemed to be controlled by procedure as for **artificial respiration**. The patient was relieved at once. The dyspnea seemed to be most pronounced during expiration, and **compression** of the **thorax** at each expiration was kept up for an hour and a half until the patient was entirely at ease.

Kulenkamp (Deut. med. Woch., Aug. 12, 1909).

In the cases with high blood-pressure, the latter should be reduced by **bleeding**, **counterirritation**, or drugs. Atropine should not be used in the high-pressure type. Cases with low blood-pressure should receive drugs which raise it. **Inhalation of oxygen** is harmless, and often gives temporary relief. **Morphine** is decidedly beneficial in any type. Miller and Matthews (Arch. of Int. Med., iv, 356, 1909).

Three cases are on record in which **vaginal Cesarean section** was done to relieve fulminating edema of the lungs. In the writer's own case the condition developed suddenly at the 8th month; the patient lay in coma, and pulseless at times. She began to breathe better immediately after the operation, and was soon convalescent. Mossini (Zent. f. Gyn., Jan. 21, 1911).

When, at the earliest threatening of paroxysmal pulmonary edema, **ammonium carbonate** has been immediately administered, an injection of **morphine sulphate**, $\frac{1}{4}$ grain (0.015 Gm.), with **atropine sulphate**, $\frac{1}{250}$ grain (0.00027 Gm.), may be very efficacious. This may be followed later by injections of **strychnine** and **nitroglycerin**. Chloroform also controls attacks, but because of its possible dangers in heart disease can hardly be recommended. Relief is also obtained from **venesection**. Stengel (Progressive Med., Sept., 1911).

A **lactovegetarian diet** and **digitalin** recommended. Then, to reduce arterial tension, the writer prescribes thus:—

R *Sodii nitritis* gr. xv (1 Gm.).
Sodii lactatis 3j (4 Gm.).
Sodii silicatis 3ss (2 Gm.).
Potassii bicarb. 3ij (8 Gm.).
Aqua destillata ... f3iv (120 c.c.).

S. Sig.: Three or four tablespoonfuls every hour for four hours.

A. Robin (Med. Press and Circ., Feb. 21, 1912).

In severe cases, for immediate relief to the overtaxed right side of the heart, **venesection** seems the only sure and

rational method. In the less severe cases **cardiotonic** and **vasodilator drugs** are of value, the action of the latter simulating the removal of a small amount of blood; if these fail, **venesection** is indicated. Southwood (Med. Jour. of Austral., Aug. 26, 1922).

Eckstein and Noeggerath have lately shown the good effect in pulmonary edema of **opening the radial artery** instead of **venesection**. The latter is too indirect a method of relieving the left ventricle of its excess of blood. The best procedure would be direct puncture of the left ventricle and removal of 300 to 400 c.c. of blood, together with intracardiac injection of a stimulant. For practical purposes, however, the author recommends taking the blood from the artery. W. Weitz (Klin. Woch., Feb. 25, 1922).

Arrest of pulmonary edema in a girl poisoned with carbon monoxide by intravenous injection of 5 c.c. (80 minims) of a 5 per cent. solution of **calcium chloride**. H. Zimmer (Deut. med. Woch., Jan. 4, 1924).

Intravenous **calcium chloride** injections tried in 22 cases. Prompt arrest of the rattling râles, sometimes after a single injection, followed, probably due to reduction of the permeability of the capillary walls in the lungs. M. John (Deut. med. Woch., Apr. 4, 1924).

In pulmonary edema attending acute or chronic nephritis, **catharsis** and **diaphoresis** may be effective in prolonging life.

PULMONARY ATELECTASIS.

DEFINITION.—Atelectasis is a congenital or acquired inability adequately to expand all the pulmonary air-cells, and results in imperfect oxygenation of the blood. The congenital form, or "blue baby," is treated under **NEWBORN, DISORDERS PECULIAR TO (q.v.)**.

SYMPTOMS.—The symptoms of the acquired form depend upon the degree of involvement of the respira-

tory tract. If but a few lobules are collapsed, compensatory action of other parts of the lung annuls the deficiency. If, however, the portions involved compromise about one-eighth of the respiratory capacity, there is dyspnea and imperfect oxygenation. Atelectasis is always a secondary condition and its symptoms are generally masked by those of the primary disease. It may arise in the course of bronchopneumonia, and not be recognized unless it becomes very extensive. *Respiration* is increased in frequency and is labored, being performed by the upper and anterior portions of the lung. The *pulse* is small, rapid, and feeble. The *skin surface*, especially of the extremities, is cool.

DIAGNOSIS.—Atelectasis is to be mainly differentiated from pulmonary embolism, pneumonia, and pleurisy.

Pulmonary Embolism.—In this disorder there is pain, bloody expectoration, and evidences of a febrile process that does not exist in atelectasis.

Lobar Pneumonia.—In the croupous form there is pain, marked crepitus, and high fever following chill. In atelectasis, however, we have a characteristic inspiratory retraction of the lower parts of the chest and smaller areas of dullness.

Pleurisy.—In this affection fever is also present; friction-sounds may be heard; percussion shows circumscribed area of flatness, shifting when the patient's position is changed.

This affection is very often met with in bronchopneumonia, especially in children.

ETIOLOGY.—Acquired atelectasis usually occurs as the result of a condition involving reduction of the lumen of the respiratory tract. For-

eign bodies may thus cause atelectasis by preventing the ingress of air, while the residual air is gradually eliminated by contractions of the thoracic walls and diaphragm, or absorbed. The bronchoscope (see LARYNGOSCOPY, BRONCHOSCOPY, etc., this volume) makes it possible to locate the foreign body in most cases and should always be resorted to.

False membrane, meconium, mucopurulent masses, blood, etc., have thus brought on this distressing condition. Processes that interfere with expansion of the chest by pressing on the lung—spinal curvature and other diseases of the bony framework, tumors, effusions into the pleural or pericardial cavities, great cardiac hypertrophy, aneurism, etc.—may also bring on atelectasis.

Abdominal tumors, excessive meteorism, and ascites may exert sufficient upward pressure against the diaphragm to compress the lower lobes of the lung. Any condition that weakens and obstructs the inspiration may cause this condition, such as certain cerebral disorders, pneumogastric paralysis, and paralysis of the chest walls. Thoracic deformities, such as pronounced kyphoscoliosis and the so-called "aplasia of the lungs," may produce pulmonary atelectasis. Kyphoscoliosis rarely causes true atelectasis, especially if it arises in youth, owing to the natural retractility of the lung. It may, however, interfere with lung expansion and growth.

PATHOLOGY.—The atelectatic areas—though hepatized, "carnified," or firm—do not show histological change, barring, perhaps, slight dilatation of the vascular supply. Viewed through the pleura, the surface is

smooth, depressed, and of a bluish-red color; on section the affected area appears brownish red. The collapsed cavities, whatever be their size, can

occur as a complication of capillary bronchitis. Pertussis and widespread bronchopneumonia may also occur as causes.

PROGNOSIS.—The prognosis varies according to the extent of the area involved. When small areas are atelectatic, recovery is usual, but extensive reduction of the respiratory capacity is seldom recovered from. When secondary to pertussis and extensive bronchopneumonia, it is very fatal. When due to compression by pyopneumothorax, tumors, etc., the prognosis is grave. In premature births the chances are greatly against the infant. The same is the case when atelectasis is the result of some pulmonary disorder.

Complications, especially pulmonary tuberculosis, pleurisy, and bronchopneumonia, are frequently observed in these cases and greatly compromise the issue. When atelectasis is due to pressure and occurs as the result of exudations into the pleura, aneurism, tumors, etc.,—the prognosis is very unfavorable. Emphysema sometimes presents itself in atelectatic infants, but, as a compensating factor, its presence increases the respiratory area.

Atelectasis due to foreign bodies is no longer as fatal as it used to be before the introduction of the bronchoscope, which in many instances makes it possible to locate the foreign body and to remove it.

TREATMENT.—The treatment is that of the primary disease. *Capillary bronchitis*, generally followed by collapse of the lobules, demands close attention; prophylactic measures are of prime importance. The patient should practise **deep breathing at regular intervals**; his position in bed



Method of resuscitation. (Dew.)

always be inflated with a blowpipe, as shown by Legendre and Bailly. The affected parts are non-crepitant, sink in water, and are resistant under section. When causative disorders are present, the post-mortem evidences vary accordingly.

Collapse of the lobules sometimes

should be frequently changed so as not to lie in one position too long. A valuable prophylactic measure is a stream of cold water applied over the neck. The inhalation of compressed air has given good results.

In *kyphoscoliosis* tepid baths do good. The heart condition requires close attention, and cardiac stimulants are demanded by the first loss of compensation or when one is unable to obtain compensation. An important indication in this disorder is to increase as much as possible the vital activity of the patient. Gentle massage under warm bedclothes, the friction being always in the direction of the heart, tends greatly to increase the activity of the circulation. Laborde's method of rhythmical traction of the tongue is said to be valuable. Oxygen inhalations would seem to be indicated, though care should be taken to avoid overstimulation, lest pulmonary hyperemia follow. Pure air is essential in such cases. A little brandy, a few drops in sugar and water, given from time to time, is generally recommended. Tonics—strychnine especially—are of value. Nutritious, though easily digested food, when the child is old enough, is of great importance as a curative factor to antagonize the vital adynamia that lies back of the trouble.

The following method of resuscitation has been advocated by Dew: The infant is grasped with the left hand, the neck resting between the thumb and forefinger (Fig. 1), the head falling far backward. The upper portion of the back and scapulæ will rest in the palm of the hand, the other three fingers being inserted in the left axilla, raising it upward and outward. Next, the knees are grasped

(Fig. 2) so that the right one will rest between the thumb and forefinger, the left between the forefinger and middle finger. The back of the thighs will rest in the palm of the operator's hand. Next, the pelvis and lower extremities are depressed (Fig. 3), while the left hand gently bends the dorsal region of the spine backward. To excite expiration the movement should be reversed, the head, shoulders, and chest being brought forward and the ribs closed upon each other. At the same moment the thighs are brought forward and rested upon the abdomen.

In Minkévitch's procedure, the infant is placed in a sitting posture on a table, with the legs extended and separated; the physician, standing behind, passes one hand into each axilla, the thumbs resting on the scapulæ, and the other fingers being applied to the front of the thorax; the trunk is then bent forward toward the angle between the separated legs, while, at the same time, the thorax is compressed by the operator's hands. The lungs are thus emptied. The body is now brought back into a horizontal position; the chest thereupon expands.

Method of expanding one lung by means of the other, applicable in the treatment of various pleural conditions and deformities of the thorax. It is illustrated by a case of wide, gaping wound of the thorax, showing the right lung completely collapsed. The patient was made to blow air into a spiroscope with the outlet tube partially closed; some of the air passed into the collapsed lung, the complete expansion of which could be observed through the wound. This exercise was repeated 100 times a day and had a most beneficial effect on the lung, pending the slow repair of the wound. J. Pescher (Bull. de l'Acad. de méd., Nov. 1, 1921).

PNEUMONOKONIOSIS.

DEFINITION AND VARIETIES.

—This is a term applied to the pro-

liferative interstitial inflammation of various pulmonary structures caused by the continued inhalation of dusts of different kinds. The three principal forms of pneumonokoniosis are *anthracosis*, or coal-miners' disease, due to the inhalation of coal-dust; *chalicosis*, or stone-cutters' phthisis, brought on by the inhalation of mineral dusts, and *siderosis*, due to the inhalation of iron oxide and other metallic particles. Clinically, pneumonokoniosis may be considered as a combination of chronic bronchitis, emphysema, and phthisis, which not infrequently assumes the tuberculous type.

SYMPTOMS.—The manifestations of the three forms of pneumonokoniosis are practically similar. Three stages may be distinguished. During the first there is general uneasiness, anorexia, loss of flesh, paroxysmal cough, and expectoration, varying to a degree, in color, with the kind of dust inhaled. In anthracosis the sputa are black, in chalicosis they are grayish black, while in siderosis they are red. In all three forms hemoptysis usually occurs, but this symptom is more frequently observed, and the hemorrhages are likely to be more copious in chalicosis. Auscultation shows that the vesicular breathing murmur is lessened during this stage, while vocal resonance is enhanced; sibilant râles are usually detectable. The signs of chronic bronchitis become clearly defined during the second stage, and dyspnea and vomiting are now added to the symptoms already outlined. The sputa not only show their characteristic coloring, but they become mucopurulent, while the hemoptyses become relatively more frequent and copious. Symptoms of emphysema are now

superadded, and the dyspnea becomes asthmatic in character. The third stage is characterized by rapidly increasing anemia; cavities may then usually be detected, along with all the symptoms of pulmonary tuberculosis, with all its attending manifestations, night-sweats, diarrhea, hectic fever, intense dyspnea, and copious expectoration in which the tubercle bacillus is often found, and the patient succumbs. The third stage may not be reached, however, if the patient is relieved of the exposure to the causative elements in time; on the other hand, the usual manifestations may be replaced by those of some other local disease, particularly lymphosarcoma or other malignant growths of the lung.

An acute form of pneumonokoniosis due to the inhalation of phosphate meal has been reported. A diffuse pneumonia affecting principally the lower lobes occurs, the symptoms and prognosis of which are those of lobar pneumonia.

ETIOLOGY.—Anthracosis not only occurs among coal-miners, but also among laborers who inhale much coal-dust. Molders of bronze, iron, and copper also suffer when coal-dust is employed by them. Chalicosis is observed among stone-cutters, knife- and axe-grinders, mill-stone makers, and potters particularly. Siderosis occurs in those who inhale iron filings and the oxide of iron, polishers, gold-beaters, dyers, blacksmiths, and other crafts in which iron is more or less utilized. It is observed also among those who inhale vegetable dust, as in grain-shovelers, cotton-spinners, cigar-makers, etc.

PATHOLOGY.—The inhalation of air thickly laden with the foreign

agents mentioned, after a prolonged period of exposure, gradually weakens and finally overcomes the physiological functions calculated to protect the bronchial mucosa. The ciliated epithelium, the phagocytes, and the mucous and alveolar cells represent many structures upon whose integrity these functions depend. When these cannot be performed, the mucous membrane of the respiratory tract is penetrated and the foreign bodies invade the lymph-spaces, which represent a second barrier and are capable of disposing of comparatively enormous quantities of intruding substances. When this line of defense is overcome, however, many particles are carried to the lymph-nodules surrounding the bronchi and the blood-vessels and to the interlobular septa under the pleura, where they accumulate between the tissue-elements, and, through the larger lymph-channels, to the substernal, bronchial, and tracheal glands, in which the stromacells of the follicular cords dispose of them permanently and prevent them from entering the general circulation (Arnold). When the pigmented bronchial glands become adherent to the pulmonary veins, however, the foreign particles may invade the general circulation and be found in remote organs, the liver and spleen especially (Weigert).

When the limit of tolerance is reached, an interstitial sclerosis begins in the bronchial glands and periarterial lymph-nodules. These gradually harden, and coalesce until large fibroid areas—cirrhotic masses—are formed in various parts of the organ. *Post mortem*, such masses, when cut, are quite resistant, and sink in water and color it black. The fingers of the

operator become blackened likewise, the cut surfaces appearing either black or marble-like. The bronchi are seldom found dilated, but the finer arterial supply is often obliterated, and cavities containing a dark fluid are formed, mainly through the arrest of nutrition. When the latter communicate with the bronchi their walls usually ulcerate. The pleura is often thickened, and lesions of the right heart are often observed.

DIAGNOSIS.—A history of prolonged exposure to some form of dust, followed by symptoms, is significant. Repeated sputum examinations for foreign particles and for the exclusion of tuberculosis by absence of tubercle bacilli are in order. X-ray examination is of value; care is to be taken, in this connection, not to assume that a dense mottling in the lungs always represents a miliary tuberculosis.

The first X-ray indication of silicosis in miners is accentuation of the hilum and larger bronchial shadows, owing to fibrosis. Further fibrosis brings out the shadows of the smaller tubes, forming a linear network, usually most marked toward the right base. The next stage is the apparent segmentation of the linear shadows, which present themselves as numerous small, closely aggregated miliary nodules; these, as the disease advances, grow in size but decrease in apparent number. The grosser indication of a tuberculous complication is one or more areas of clouding, usually unilateral at first. The heart shadow in silicosis tends to become more and more vertical, but not so much so as in simple tuberculosis. W. Steuart (*Arch. of Rad. and Electr.*, Feb., 1923).

TREATMENT.—Unless removal to hygienic surroundings early in the history of the case can be carried out, pneumonokoniosis progresses stead-

ily. Anthracosis advances slowly, but chalicosis is usually fatal after three or four years. In siderosis the duration of life is somewhat longer. If the patient cannot be removed elsewhere and finds himself obliged to continue his occupation, the wearing of appropriate **masks** or **respirators** may stay the progress of the disease. **Free ventilation** of shops, mines, etc., is also prophylactic in this particular; but total **change of occupation** is the only absolute protective. The disease is often arrested when this can be done. **Potassium iodide**, and the measures indicated in chronic bronchitis (*q.v.*) and emphysema (*q.v.*) from other causes, have given excellent results when hygienic surroundings are within the reach of the patient. It may be advantageous to increase expectoration by the use of such drugs as **ammonium chloride** or **carbonate**, **ippecac**, and **apomorphine**. When pulmonary tuberculosis develops, the treatment must be modified to meet the new conditions.

Counihan has recommended **fibrolysin** (a chemical combination of sodium salicylate and thiosinamine) in the treatment of miners' phthisis, and had success in ameliorating the symptoms. The improvement is shown after the third or fourth injection, and is evidenced by a feeling of less discomfort, less cough, and freer expectoration. The patient generally sleeps longer and more comfortably and eats better. At the end of six weeks he looks decidedly better and loses the pinched, blue expression. Counihan used Mendel's preparation in ampules of 2.3 c.c. each, injected 3 times a week. Given hypodermically, it is practically painless.

SYPHILIS OF THE LUNGS.

SYMPTOMS.—The symptoms of this condition are either those of a simple bronchial catarrh or are suggestive of pulmonary tuberculosis, such

manifestations as fever, expectoration, sweats, and loss of weight being noted. Areas of dullness, with bronchial breathing and increased vocal resonance, are likely to be found, and the prolonged course of the affection is likewise suggestive of tuberculosis.

ETIOLOGY AND PATHOLOGY.

—The condition, which is due to *Spirochæta pallida*, is an uncommon one, except in its congenital form. In the secondary stage of syphilis the pathological state present is merely one of catarrhal inflammation of the bronchi. In the more frequent cases occurring in the tertiary (or late secondary) stage gummatus infiltration of the submucous tissue of the trachea and bronchi is not uncommon. In the lung-tissue itself gummata may also occur, singly or in numbers, and ranging in size from that of a hemp seed to that of a goose egg. Such lesions occur oftenest in the interior portions of the lung and at the bases, the latter being a feature distinctive of syphilitic as against tuberculous lung disease. Syphilitic bronchopneumonia is a possible condition, and fibroid changes have been ascribed to syphilis as follows: (1) Thickening extending from the hilus around the bronchi and vessels; (2) isolated masses of fibroid tissue in various parts of the lung; (3) diffuse changes occupying the greater part or the whole of the lung (Roussel). White radiations extending from the gummata out into the neighboring tissues have been noted.

DIAGNOSIS.—In the early stages distinction between lung syphilis and tuberculosis is extremely difficult. Later, the continued absence of tubercle bacilli from the sputum, the negative tuberculin (von Pirquet)

test, and especially the prompt favorable effect of antisyphilitic treatment will prove significant. If no tubercle bacilli appear in the sputum after administration of iodides, the presence of a condition other than lung tuberculosis may be strongly suspected. In regard to the Wassermann reaction, it should be borne in mind that this test may be positive in tuberculosis in the absence of syphilis, although if non-cholesterinized antigens are used the probability of such an error is very slight.

Other diseases which must be thought of in the differential diagnosis are tumor of the lung and blastomycosis.

In pulmonary syphilis cough is often slight. Sputum varies in amount with the cough. Hemoptysis may occur. Dyspnea is more common than in tuberculosis. Pain in the chest and hoarseness may be noticed. Fever, sweating and emaciation are rare. As complications, pulmonary gangrene and pyopneumothorax are rare, but syphilis and tuberculosis may coexist. Aside from the usual diagnostic tests, a search of the sputum with dark-field illumination is worth trying. In any case of suspected lung syphilis a thorough course of antisyphilitic therapy is justified. C. P. Howard (*Amer. Jour. of Syph.*, Jan., 1924).

TREATMENT.—The measures customarily employed in syphilis—**arsphenamin, mercury, potassium iodide**, etc.,—are indicated in these cases, and under their use the symptoms rapidly disappear.

TUMORS OF THE LUNGS.

The lungs are subject to involvement by carcinoma, sarcoma, adenocarcinoma, subpleural enchondroma, myxoma, osteoma, fibroma, and dermoid growths. In the great majority of cases of malignant tumor the growth is secondary.

SYMPTOMS.—Among the chief symptoms of malignant lung involvement are cough, expectoration, pain, and swelling of the arms and a livid aspect of the face, due to obstruction of vessels by the tumor. Dark, reddish sputum and fever are symptoms the result of a pneumonic process taking place as a reaction around the seat of malignant invasion.

Difficulty of breathing, sometimes marked, may result from pressure of the tumor mass or masses on the trachea or bronchi, aphonia from compression of the vagus or recurrent laryngeal nerves, and even the heart itself may be displaced. The physical signs of pneumonia may be elicited upon percussion and auscultation, and signs of pleurisy may also exist. Both dyspnea and emaciation are likely to appear early. Cachexia supervenes and terminates in death, generally in eight months, unless encroachment on the vessels or the respiratory passages has already caused an acute fatal ending at an earlier period.

In the presence of benign tumors of the lung the symptoms are similar, with the exception that cachexia is absent and exitus delayed.

PATHOLOGY.—The commonest tumor condition in the lungs consists in the presence of a number of whitish nodules of carcinoma or sarcoma, about $\frac{1}{2}$ inch in diameter, disseminated in one or both organs. The primary seat of malignant disease in these cases is usually the breast, and, correspondingly, secondary lung tumor is commoner in the female than in the male sex, whereas in the case of primary lung tumor the two sexes are affected with approximately like frequency.

Primary carcinoma of the lung may be either medullary, scirrhus, epitheliomatous, melanotic, or colloid in type, and generally occurs in the posteroexternal portion of the upper pulmonary lobe in the form of a whitish nodule ranging in size from that of a plum to that of a large orange. The bronchial glands and pleura may be secondarily involved from this type of tumor, or the growth may be peribronchial from the outset, occurring in nodules of varying size dispersed along the bronchi and bronchioles, and leading also to involvement of the lymph-nodes at the pulmonary hilus.

The striking increase in the number of tumors of the lung since the last influenza epidemic suggests some relation between these two conditions. Analyzing 24 cases of primary lung cancer the writers point out that a very varied pathologic picture is presented by these tumors. Metastases occur early and are very widespread. Origin from bronchial mucosa appears to be most frequent and that from the alveolar epithelium very rare. Grove and Kramer (*Amer. Jour. Med. Sci.*, Feb., 1926).

DIAGNOSIS.—X-ray examination permits of earlier diagnosis than any other proceeding. Otherwise, the diagnosis is made from observation of the symptoms already mentioned, persistence of such manifestations over a long period being suggestive, especially if a primary growth is known to be present elsewhere. The supra- and infra-clavicular lymph-nodes may be significantly enlarged.

TREATMENT.—The X-ray should be tried in these cases, as it has given striking palliative results in some instances. Attempts at **operative removal** have been made, but there is great difficulty in reaching a malignant lung tumor sufficiently early to permit of

lasting recovery. The patient should, in any case, be rendered comfortable by the use of **narcotic drugs**. **Paracentesis thoracis** may relieve pressure symptoms and dyspnea for a time. For pleuritic pain the **chest** may be **strapped**.

Case in which what appeared to be a large tumor at the hilus, supposed to have followed a severe attack of influenza, and accompanied by painful axillary glands, chest pain, and pressure on the bronchi, was reduced by a half, with disappearance of cough and hemoptysis, by **deep X-ray treatment**—5 H. units per hour for 15 hours in 15 sittings distributed over 3 weeks. Thiroloix and Pierquin (*Bull. Soc. méd. des hôp. de Paris*, July 13, 1922).

In malignant pulmonary metastases, the writers advocate **deep Roentgen-ray** therapy when metastases cannot be demonstrated in the remainder of the body. The best results were obtained in the embryonal type of sarcoma (angiosarcoma), while the fibroblastic, adult types, especially when rich in paraplastic structures, were refractory. The nearer the sarcoma approaches the undifferentiated embryonal type, the better the chance of success. Evans and Leucutia (*Amer. Jour. of Roentgenol.*, Jan., 1924).

Case of a woman in whom a clearly outlined circular, non-expansile mass of the size of a small orange in the right hilus was detected by X-ray. Puncture revealed a hard-walled cyst containing yellowish fluid, which was later detached from the pleura and lung by blunt dissection and **removed**. Recovery followed. Ström (*Acta radiol.*, Apr. 10, 1924).

CHARLES E. DE M. SAJOUS,
Philadelphia.

LUNGS, INJURIES AND SURGERY OF. See CHEST, INJURIES AND SURGICAL DISEASES OF.

LUPULUS (OR HUMULUS) AND LUPULIN.—Lupulus, or hops, consists of the carefully dried strobiles, or

fruit, of *Humulus lupulus*, of the family Moraceæ, bearing their natural glandular powder (trichomes). The glandular powder, or *lupulin*, detached from the hops by sifting, occurs as a bright, light-brownish-yellow (becoming yellowish brown), mobile, granular, resinous powder, having a strong odor of hops and a strongly aromatic and bitter taste. It is of low specific gravity, and floats on water. Lupulin contains a brownish-yellow fluid, which dries to a resinous mass. It yields a tasteless resin, a wax known as *myricin* (myrocyclic palmitate), and the bitter *lupamaric* or hop-bitter acid.

PREPARATIONS AND DOSE.—

Recognized in the National Formulary are:—

Humulus, N. F. (hop). Dose, 30 grains (2 Gm.).

Fluidextractum humuli, N. F. (fluidextract of hop). Dose, 30 minims (2 c.c.).

Tinctura humuli, N. F. (tincture of hop). Dose, $\frac{1}{2}$ to 2 fluidrams (2 to 8 c.c.).

Lupulinum, N. F. (lupulin), soluble in ether to the extent of 60 per cent. Dose, 3 to 15 grains (0.2 to 1 Gm.).

Fluidextractum lupulini, N. F. (fluidextract of lupulin). Dose, 5 to 20 minims (0.3 to 1.25 c.c.).

THERAPEUTICS.—Lupulin and humulus have been credited with some hypnotic power, and have been used for purposes of nervous sedation in the treatment of **hysteria**, **insomnia**, general **nervousness**, and even **delirium tremens**. Their continuous ingestion does not appear to be followed by any undesirable after-effects.

Stern found lupulin of special value in the **functional disturbances** of the **gastrointestinal tract**, including sensory as well as motor and secretory neuroses, **nervous anorexia**, **hyperesthesia** of the **gastric mucosa**, and **cardialgia**. He prescribed lupulin

in 5-grain (0.3 Gm.) capsules half an hour before meals, either alone or in conjunction with berberine phosphate, capsin, silver nitrate, monobromated camphor, iron and strychnine citrate, nux vomica, cinchonidine sulphate, etc., according to indications. In **intestinal neuroses** lupulin, in doses one-half again or twice as large as used for the stomach, also proved useful in Stern's hands.

Hop tea, consisting of an infusion of $\frac{1}{2}$ ounce (15 Gm.) of hops in a pint (500 c.c.) of boiling water, has proved useful at times in **flatulence**, mild **diarrhea**, and **atonic gastric states**. Given in doses of $\frac{1}{2}$ to 1 wineglassful before meals, it acts as a stomachic.

In **irritation of the kidneys** or **bladder**, and in **priapism**, lupulin appears to have been of some utility. W. and S.

LUPUS. See TUBERCULOSIS OF THE SEROUS MEMBRANES AND SKIN.

LYCETOL. See PIPERAZIN.

LYMPH-GLANDS, INJURIES AND DISEASES OF. See THYMUS, LYMPHATICS, AND MEDIASTINUM, DISEASES OF.

LYMPHANGIECTASIS. See THYMUS, LYMPHATICS, AND MEDIASTINUM, DISEASES OF.

LYMPHANGIOMA, See THYMUS, LYMPHATICS, AND MEDIASTINUM, DISEASES OF.

LYSIDIN. See PIPERAZIN.

LYSOL. See TAR.

M

MADURA FOOT (MYCETOMA).—A condition of the foot due to invasion by *Madurella* (*Streptothrix*) *mycetomi*, usually through a scratch or abrasion of the skin, causing enlargement, deformity and finally destruction of the member.

SYMPTOMS.—After an incubation period of from ten to thirty days following the cut or injury, pain or swelling appears at the site of the primary lesion, which swelling becomes hard and a bleb forms on the surface, which bursts and leaves a small

opening, discharging an oily, rarely sanious, thin, offensive pus, in which are the granules characteristic of the fungus. The dorsum of the foot becomes studded with nodules and openings, which latter lead into sinuses penetrating deeply into the tissues, even into the bones. The disease has no tendency to heal, and the patient dies from exhaustion or diarrhea after from ten to twelve years.

Three varieties are to be distinguished clinically, the yellow or ochroid, the black, and the red, named from the color of the granules found in the discharge. The ochroid is the most common, the red the least. A number of cases have been reported from Texas.

TREATMENT.—Prophylaxis consists in guarding against wounds from pieces of wood, stones, thorns, etc., by wearing sandals, shoes, or boots. Any wounds received should at once be thoroughly cleansed, carefully dried, and then mopped with tincture of iodine.

The treatment proper is surgical, and consists of curetting or excision if the process be localized; otherwise, of amputation through healthy tissues.

According to Noc and Jouenne, in early cases potassium iodide and neoarsphenamin, with collargol locally, curettage, and disinfection with an ethereal solution of iodoform, may yield a cure.

W.

MAGNESIUM.—Magnesium is a metal of the alkaline earth group, light and having the appearance of silver. When rolled in thin plates or ribbons, magnesium can be ignited, and burns with a brilliant, white flame, giving off a dense white smoke, which consists of the oxide of magnesium. Magnesium oxide and various salts are official.

PREPARATIONS AND DOSE.—*Magnesiæ oxidum*, U. S. P. (Magnesium oxide; magnesia; light magnesia; calcined magnesia) [MgO], occurs as a very light, bulky, fine, white powder, with a slight earthy taste, and slowly absorbs moisture and carbon dioxide

on exposure to the air. It is almost insoluble in water, and insoluble in alcohol, but dissolves in dilute acids. When moistened and placed in contact with red litmus paper it exhibits a faintly alkaline reaction. Stirred with 15 parts of water and allowed to stand half an hour, it forms a gelatinous mass of magnesium hydroxide. Dose, 4 to 60 grains (0.25 to 4 Gm.); official average dose, as antacid, 4 grains (0.25 Gm.); as laxative, 45 grains (3 Gm.).

Magnesiæ oxidum ponderosum, U. S. P. (heavy magnesium oxide; heavy magnesia; Husband's magnesia) [MgO], occurs as a heavy, fine, white powder, with the same properties as the preceding, except that it fails readily to unite with water to form a gelatinous hydroxide. It contains, after ignition, not less than 96 per cent. of MgO . Dose, as of the preceding.

Magnesiæ carbonas, U. S. P. (magnesium carbonate) [approximately $(MgCO_3)_4 \cdot Mg(OH)_2 + 5H_2O$], occurs in light, white, friable masses or a bulky, white powder, with a slight earthy taste, and permanent in the air. It is practically insoluble in water, more soluble in carbon dioxide water, insoluble in alcohol, but soluble in dilute acids. When strongly heated it is converted into magnesium oxide. Dose, 5 grains to 2 drams (0.3 to 8 Gm.); official average dose, as antacid, 10 grains (0.6 Gm.); as laxative, 2 drams (8 Gm.).

Magnesiæ sulphas, U. S. P. (magnesium sulphate; Epsom salt; bitter salt) [$MgSO_4 \cdot 7H_2O$], occurs in small, colorless needles or rhombic prisms, with a cooling, saline, and bitter taste, soluble in 1.3 parts of water at 25° C. and in 0.2 part of boiling water;

sparingly soluble in alcohol. Dose, 1 dram to 1½ ounces (4 to 48 Gm.); official average dose, 4 drams (16 Gm.).

Liquor magnesiæ citratis, U. S. P. (solution of magnesium citrate), is made by dissolving 35 Gm. of citric acid in 150 c.c. of hot distilled water and, after addition of 15 Gm. of magnesium carbonate previously mixed with 100 c.c. of distilled water, stirring until it is dissolved. Syrup, 60 c.c., is then added, the mixed liquids heated to boiling, 0.1 c.c. of oil of lemon (previously triturated with 5 Gm. of purified talc) added, and the mixture filtered while hot into a strong bottle previously rinsed with boiling water. Enough boiled distilled water is now added to make 350 c.c., the bottle stoppered with purified cotton, the solution allowed to cool, 2.5 Gm. of potassium bicarbonate dropped in, the bottle at once stoppered securely, and the solution shaken occasionally until the bicarbonate is dissolved. The bottle should be kept on its side in a cool place, preferably in a refrigerator. Dose, 12 fluidounces (350 c.c.).

Magma magnesiæ, U. S. P. (milk of magnesia), is made by treating a solution of magnesium sulphate in water with sodium hydroxide, and contains as a suspension in water 7 per cent. of magnesium hydroxide in a finely divided state. Dose, as antacid, 1 fluidram (4 c.c.); as laxative, 4 fluidrams (15 c.c.).

Pulvis rhei compositus, U. S. P. (compound rhubarb powder). For ingredients see RHUBARB. Dose, ½ dram (2 Gm.).

Ferri hydroxidum cum magnesiæ oxido, U. S. P. (ferric hydroxide with magnesium oxide). For ingredients see IRON. Dose, 4 fluidounces (120 c.c.).

Infusum sennæ compositum, N. F. (compound infusion of senna; black draught). For ingredients, see SENNA. Dose, 4 fluidounces (120 c.c.).

Pulvis rhei et magnesiæ anisatus, N. F. (compound anise powder). For ingredients, see RHUBARB. Dose, for infants, 5 grains (0.3 Gm.).

PHYSIOLOGICAL ACTION.—

Locally, strong solutions of magnesium salts have been shown experimentally by Wiki to possess distinct local anesthetic power. Injected into the skin of guinea-pigs, a saturated solution of magnesium sulphate containing 0.62 Gm. of the salt in each cubic centimeter produces complete local anesthesia, generally persisting over an hour. Superficial inflammations of various kinds are, moreover, attenuated or inhibited by local application of concentrated magnesium sulphate solutions; the reason for this, however, is as yet obscure.

Whereas solutions of sodium sulphate and sodium chloride approximately isotonic with the body fluids have no anesthetic power, magnesium sulphate solutions of the same molecular concentration (about 7 per cent.) produce distinct local anesthesia. A solution of magnesium chloride of 5 per cent. strength was found to produce anesthesia of short duration; 7 to 10 per cent. solutions produced insensibility lasting somewhat over half an hour. B. Wiki (Archives intern. de pharm. et de thérap., vol. xxi, Nos. 5-6, 1912).

Introduced into the intestine, soluble magnesium salts, in particular the sulphate, exert a purgative effect probably by drawing water from the surrounding tissues through osmotic action as well as by preventing the absorption of water already present in the canal and of that introduced with the salt itself. The excessive

fluid content of the bowel then causes rhythmic intestinal segmentations (Cohnheim), which in the course of one or a few hours result in the passage of one or more watery stools; some of the solids in the intestine, however, are apt to remain behind, and therefore a saline cathartic such as magnesium sulphate may not cleanse the bowel as thoroughly as a more slowly acting vegetable cathartic that will directly excite peristalsis (Bastedo). In the stomach strong solutions of magnesium sulphate are somewhat irritating and tend to produce nausea; this effect can, however, be largely obviated by administration of the salt in an effervescent drink. In contrast to what occurs after the administration of sodium sulphate, the purgative effect of magnesium sulphate seems to increase when the same dose is repeated several days in succession.

General Effects.—*Nervous System.*—While little or no systemic effect of the ion magnesium is obtained when a magnesium compound (unless in concentrated solution) is taken by the mouth, the metal is by no means devoid of specific toxic properties, as was pointed out by Meltzer and his associates upon experimental administration of magnesium salts by parenteral routes. Injected subcutaneously, intravenously, or intraspinally, solutions of magnesium salts cause a gradually oncoming motor paresis, eventuating in complete muscular relaxation and general anesthesia. If the intoxication be further slightly augmented respiratory depression appears, and death may take place through failure of this function. These effects are ascribed to a paralyzing action of the drug on nerve-

endings, probably beginning with those of the motor nerves to striped muscle tissue (a curare-like action), but soon after involving also the sensory.

Circulation.—Magnesium salts, when present in the circulation, tend to depress the heart—in particular, the cardioaccelerator nervous mechanism, according to Matthews and Brookes. Death takes place, however, not from circulatory, but from respiratory, paralysis (peripheral). If life is maintained by artificial respiration, depression of the vasomotor center is likely sooner or later to follow.

Alimentary Tract.—That magnesium sulphate injected subcutaneously or intravenously will at times induce purgation suggests that the cathartic effect of the drug may be due not alone to osmotic action in the bowel, but to a direct stimulating effect on peristalsis. Experimental results in this connection have been conflicting. That some peristaltic stimulation occurs from small amounts cannot as yet be considered to have been disproved. Large amounts absorbed into the blood are known to paralyze the bowel.

In the purgative effect of magnesium sulphate both the magnesium and sulphate ions are active. With magnesium oxide, hydroxide, and carbonate, on the other hand, the magnesium ion alone is active as a purgative, their action being, therefore, less marked. These salts, however, act in addition as non-caustic alkalies. The gelatinous hydroxide of magnesium will saturate $1\frac{1}{2}$ times its weight of official hydrochloric acid.

Absorption and Elimination.—Though not absorbed to any significant extent from the bowel under

ordinary circumstances and as ordinarily administered, magnesium sulphate is in part absorbed when given in a concentrated solution or in dry form, or, where there is intestinal paresis, even in dilute solutions, causing general systemic depression. By whatever route introduced into the circulation, magnesium salts are eliminated to a great extent through the kidneys.

When soluble magnesium compounds are introduced into animals by another route than the gastrointestinal tract, the greater portion of the excess injected leaves the body through the kidneys in less than forty-eight hours. The intestinal path is of minor, if any, significance. A considerable quantity of magnesium may be retained in the body for periods exceeding two weeks. The increased excretion of magnesium by the kidneys is accompanied by a marked rise in the urinary output of calcium. Parenteral introduction of magnesium sulphate in dogs and rabbits is never followed by purgation. Diuresis, however, occurs. L. B. Mendel and S. R. Benedict (*Amer. Jour. of Physiol.*, Sept., 1909).

UNTOWARD EFFECTS AND POISONING.—Where sufficient absorption of magnesium into the system occurs, signs of poisoning, at times very serious, will inevitably develop. Of 10 cases of poisoning reported by Boos, 6 resulted in death. The symptoms closely resemble those witnessed in experimental poisoning of animals, and include motor weakness in the limbs, difficult respiration, mydriasis, vomiting in about one-half the cases (Boos), convulsive phenomena in occasional instances, coma, oliguria, slowing and weakening of the heart action, and death from respiratory failure. Burning pains in

the abdomen may have been experienced through local irritation by the salt taken.

Report of 10 cases of poisoning from magnesium sulphate. In 7 there was no effect. The salt, on the other hand, seemed to cause a paralysis of the bowel, so marked in 2 cases that laparotomy was performed. A marked diminution of the urine also occurred, amounting in some almost to anuria. In only 1 case was there active purging. This patient had taken the salt in several pints of beer. Convulsions and motor paralysis were observed in 2 cases. Striking depression of respiration occurred in 6 cases. Boos (*Jour. Amer. Med. Assoc.*, vol. iv, 2038, 1911).

Magnesium sulphate given by mouth as a laxative is often followed by considerable depression, particularly if it fails to cause the bowels to move. The author used the drug as a laxative in a number of children. In nearly every case it was followed by more or less marked depression. LeGrand Kerr (*L. 1. Med. Jour.*, Mar., 1914).

In most cases of poisoning catharsis has failed to take place, the salt being instead absorbed from a concentrated solution. Urine into which it is being excreted not infrequently shows a very high specific gravity—1.070 or even 1.080.

In the absence of hydremia the tendency of magnesium sulphate to be absorbed increases with the concentration of the solution, the dry salt being completely absorbed without action on the bowels. In hydremic conditions, however, the salt, even when given in very concentrated solution, is not absorbed. It appears, therefore, that the practice of giving very concentrated solutions of magnesium sulphate to deplete the system of excessive water is rational, but perhaps not without possible danger. In the absence of edema or

ascites the object of giving magnesium sulphate can be none other than to produce efficient catharsis. To obtain this without danger of intoxication, the salt is best given in solutions not exceeding 6 per cent. in strength. Above this concentration more or less magnesium sulphate is absorbed and is lost to catharsis, while its presence in the circulation is a menace to the patient's life. In the Massachusetts General Hospital the patients are given $\frac{1}{2}$ ounce (15 Gm.) of magnesium sulphate dissolved in 3 fluid-ounces (90 c.c.) of water, to be followed immediately by a glass of water. Boos (Boston Med. and Surg. Jour., July 22, 1909).

On account of the slowness of its excretion from the system magnesium sulphate is capable of producing poisoning by the cumulative action of small doses, given repeatedly in concentrated solution (Boos).

In several of the cases of fatal poisoning the amount of magnesium sulphate taken had been only 1 ounce (30 Gm.). At autopsy the most typical findings are patches of reddening on the gastrointestinal mucous membranes.

Treatment of Magnesium Poisoning.—Boos advises that in cases of suspected magnesium poisoning copious **intravenous saline infusions** be given. Dilute solutions of **calcium salts** given hypodermically may also prove of benefit. (Intravenous injection of a solution of calcium chloride in animals poisoned with magnesium sulphate frequently causes almost instantaneously a marked improvement in motor power.) **Physostigmine** (eserine) might likewise be of some use, Meltzer and Joseph having demonstrated the antagonistic action of magnesium sulphate and this drug on the nerve-endings in striped muscle.

Stimulants such as **ammonia, ether, atropine, cocaine, strychnine, and digitalis**, as well as **external heat**, are also indicated in these cases.

Case of poisoning in a boy $3\frac{1}{2}$ years of age who took a heaping spoonful of Epsom salts, thinking it to be sugar. A few minutes later he was found with pain in the stomach, nausea and retching, thirst and vomiting. When seen twenty-five hours later he was critically ill, lying on his back, with face pinched, eyes sunken, and skin pale. The mind was clear. There were intermittent colicky attacks. Temperature, 100.5° F.; pulse, 160 and small; tongue dry, with prominent papillæ; thirst intense, and the bowels had not acted. Half an ounce of urine had been passed in twenty-four hours. The abdomen was distended and rigid, and the skin markedly hyperesthetic. The catheter withdrew half an ounce of dark, muddy, very acid urine, containing no albumin. The symptoms getting worse and suggesting acute peritonitis, laparotomy was performed. About 2 pints of blood-stained serum, subsequently found sterile, were withdrawn. No cause for obstruction was found. For forty-eight hours the child seemed moribund. Subcutaneous **saline injections** were made, and $\frac{1}{2}$ grain (0.03 Gm.) of **calomel** given every hour. Finally flatus and feces passed, the bowels opened, and recovery ensued. Fraser (Lancet, Apr. 24, 1909).

THERAPEUTICS.—As **antacids** magnesium oxide, heavy magnesium oxide, and magnesium carbonate are used. Of these, the heavy oxide would seem to be, perhaps, the best. The light magnesia has the disadvantage of being bulky in sufficient doses, and magnesium carbonate is apt to give rise to flatulence on account of the carbon dioxide gas given off when it is subjected to the action of the acid of the gastric juice. The latter

objection, however, does not always hold, since the stimulating action of the carbon dioxide gas upon the mucous membrane of the stomach is at times beneficial, the drug acting as a sedative and anodyne in the treatment of **indigestion** with **sick headache** or **pyrosis**. In **diarrhea** from indigestion, with acid stools, magnesium oxide combined with rhubarb yields very satisfactory results.

Magnesium oxide, being free from taste and non-irritating, is a very desirable remedy for children. The carbonate, combined with carminatives, is especially useful in the **flatulent colic** and **diarrhea** of infants. Demers's formula is:—

℞ *Magnesium carbonate* ʒss (2 Gm.).
Tincture of asafetida gtt. xl.
Tincture of opium .. gtt. xx.
Sugar ʒj (4 Gm.).
Distilled water fʒj (30 c.c.).—M.

The dose is $\frac{1}{2}$ to 1 teaspoonful, according to age.

The antacid properties of magnesium oxide render it valuable as an antidote in cases of **poisoning** by the strong **mineral or vegetable acids**. Besides neutralizing the acids, it acts as a mechanical protective to the tissues against their corrosive action. Its value as an antidote in **poisoning** by **metallic salts** is asserted to depend upon a precipitation of many metals from the acid combined with them, thus rendering them less poisonous. In **poisoning** by **arsenic** freshly prepared magnesium hydrate has been regarded as an antidote inferior only to the official hydrate of iron with magnesium oxide (although even the efficacy of the latter has been seriously questioned by some).

As **purgatives** magnesium oxide and carbonate are often used in children.

In adults the neutral salts, the citrate and sulphate, are more generally employed. The oxide and the carbonate are hardly suitable for continuous administration, as, being insoluble, they may accumulate in the intestines and form concretions of the hydrate of magnesium. Magnesium citrate and sulphate cause little, if any, irritation, and are on that account valuable as laxatives in **enteritis**. A rather free ingestion of water at the time of administration assists their action. In **intestinal putrefaction** they are also of decided utility. In **febrile affections**, given in small doses, they exert a refrigerant and a slight diuretic action. Combined with iron, they are useful in **constipation** associated with atonic conditions. In **anemia** and **chlorosis** the following mixture is not infrequently useful as a tonic laxative:

℞ *Magnesium sulphate* ʒj (30 Gm.).
Potassium bitartrate ʒj (4 Gm.).
Dried ferrous sulphate gr. x (0.6 Gm.).
Water Oij (1000 c.c.).—M.

Sig.: One wineglassful a half-hour before breakfast each morning.

The constipation of **lead poisoning** is relieved best by magnesium sulphate as follows:—

℞ *Magnesium sulphate* .. ʒij (8 Gm.).
Morphine sulphate .. gr. j (0.06 Gm.).
Peppermint water fʒiij (90 c.c.).

M. Sig.: One tablespoonful every two hours in lead colic.

Culbertson asserts that the usual method of giving magnesium sulphate can be greatly improved upon by administering only $\frac{1}{2}$ to 1 dram (2 to 4 Gm.), dissolved, however, in a pint (500 c.c.) of water. The water aids in establishing increased peristalsis. The same dose given at bedtime acts well as a diuretic and stimulant to elimination through the skin. In

migraine magnesium sulphate should be given in doses of $\frac{1}{2}$ to 1 dram (2 to 4 Gm.) at bedtime, dissolved in a goblet of warm water.

The purgative mineral waters (Friedrichshall, Püllna, Seidlitz, and Hunyadi) owe their purgative action principally to the presence of magnesium sulphate.

In **serous effusions** (pleural, peritoneal, etc.) magnesium sulphate in doses of 1 or 2 ounces (30 or 60 Gm.) daily yields good results, especially if the amount of fluids ingested be restricted. It may be given by enema if preferred, as proposed by Watkins:

℞ *Magnesium sulphate* ʒij (60 Gm.).
Glycerin fʒj (30 c.c.).
Water fʒiv (120 c.c.).—M.

Edema and anasarca, as in **Bright's disease**, are relieved in a similar manner by magnesium sulphate. It tends to relieve the congestion of the kidneys in general anasarca and is also of value in **edema of the lungs** and **brain**, and in **ascites**. In particularly asthenic cases it should be used with caution, as it is liable further to weaken and depress the patient. In **uremia** associated with constipation magnesium sulphate is a valuable remedy.

In 17 cases of **obstinate constipation** occurring in cases of **appendicitis**, **corrosive sublimate poisoning**, **acute articular rheumatism**, **pneumonia**, **valvular disease**, **gastric cancer**, etc., the authors made hypodermic injections of from 0.5 to 5 c.c. (8 to 80 minims) of a 25 per cent. solution of magnesium sulphate. Best results were obtained by injecting under the skin of the abdomen. Good bowel movements were obtained in 14 cases. A dose of from 0.5 to 1 c.c. (8 to 16 minims) was found most effective.

The authors advocate the pro-

cedure where purgation in the usual way is impossible, where rectal administration is ineffective, or where it is desirable to affect the intestinal musculature rather than the intestinal mucosa. Thus, it would appear to be of value in cases of **uremic coma**, **tonsillar abscess**, **intestinal paresis**, **intestinal obstruction**, and in patients who are unable to retain anything on their stomach. A. Robin and M. Sourdel (Bull. et mém. de la Soc. méd. des Hôp. de Paris, June 20, 1912).

Administration of magnesium sulphate is of assistance to **lessen** the **mammary secretion**, where this is desired, in nursing mothers.

Diarrhea due to **fecal impaction** is best relieved by small doses of magnesium sulphate given every hour. The drug is also useful in **dysentery**, combined with aromatic sulphuric acid and tincture of opium. In **acute dysentery** it will often overcome the fever and tenesmus, and remove the blood and mucus from the stools. Leahy has advised the use of the following: Saturate 7 fluidounces (210 c.c.) of water with a sufficient quantity of magnesium sulphate, and add 1 fluidounce (30 c.c.) of diluted sulphuric acid. Of this give a tablespoonful (15 c.c.) every hour or two in a wineglassful of water until it operates. Morphine may be added, or starch enemata with laudanum used.

In persistent **diarrhea** due to indigestion in cases of **tuberculosis** Robin recommends the following combination:—

℞ *Magnesii hydroxidi* ʒiss (6 Gm.).
*Bismuthi subnitrat*is ... ʒss (2 Gm.).
Sodii bicarbonatis ʒij (8 Gm.).
Calcii carbonatis præ-
cipitati,
Sacchari āā ʒss (16 Gm.).

Ft. in chart. no. xxiv.

Sig.: One powder after each meal.

In **rectal disorders** magnesium sulphate in moderate doses is of great value, as it liquefies the fecal passages and renders them less irritating. In **cancer** or **stricture of the rectum**, **hemorrhoids**, and **fissure of the anus** this is very desirable. Magnesium sulphate, as well as other salines, will act painlessly upon the bowels of a patient fully under the influence of opium, which renders them especially useful in **atony of the rectum**.

The unpleasant taste of magnesium sulphate may be conveniently disguised by the addition of a small amount of fluidextract of licorice or by boiling it with or giving it in coffee. For general use 4 ounces (125 Gm.) of magnesium sulphate may be dissolved in 4 fluidounces (125 c.c.) of lemon or other syrup, and enough water added to make 1 pint (500 c.c.). The dose is a wineglassful or two.

As a **general sedative** magnesium sulphate has acquired some reputation. Its value in this direction has been especially emphasized by Weston and Howard, who inject subcutaneously or intramuscularly 2 c.c. (32 minims) of a 50 per cent. solution, repeated at $\frac{1}{2}$ hour intervals when necessary.

Finding the C. P., U. S. P., and "reagent" magnesium sulphate would not give a clear, colorless solution, the writers recrystallized the crude salt 3 times to obtain a pure product, made a 50 per cent. solution of the salt with its water of crystallization, and sterilized it in the autoclave. No local pain or sloughing occurred in over one thousand injections. The drug was used mainly in the **insane**, when suffering from hallucinations, talking loudly, shouting or screaming, refusing to stay in bed, and molesting other patients. In 82.7 per cent. of cases quiet was induced in 15 to 30 minutes and sleep for 5 to 10 hours followed. In 6 per cent. repetition of

the dose was required. The drug proved an excellent substitute for morphine and hyoscine in many cases. It was also used in persons not insane suffering from severe **pain**, with very gratifying results. No change in pulse rate due to the magnesium was observed. P. G. Weston and M. L. Howard (Amer. Jour. Med. Sci., Mar., 1923).

Combination of 20 to 30 minims (1.3 to 2 c.c.) of a 25 or 50 per cent. solution of magnesium sulphate with morphine by hypodermic injection has been asserted greatly to increase the efficiency of the morphine in relieving pain and producing sleep. Beckman has, however, on the basis of experimental work, called into question the actual occurrence of such a potentiation.

Value of magnesium sulphate in conjunction with morphine for **obstetrical analgesia** pointed out. Two cubic centimeters (32 minims) of 25 per cent. magnesium sulphate solution hypodermically with $\frac{1}{8}$ grain (0.008 Gm.) of morphine sulphate give greater relief than $\frac{1}{4}$ grain (0.015 Gm.) of morphine given alone. Varying amounts of relief were afforded in 93.4 per cent. of the women receiving these drugs, and no unfavorable effects on labor nor on the condition of the mother or child could be discerned. T. W. Adams (Amer. Jour. of Obst. and Gyn., Sept., 1924).

Attention has been directed, largely owing to the observations of Lyon in diseases of the biliary tract, to the effect of magnesium sulphate on the **biliary function** of the liver. Introduction of the salt through the duodenal tube having been observed to induce a flow of bile, several theories as to its mode of action have been advanced: (1) That it increases bile flow through osmotic effects which overcome local swelling and congestion and thus facilitate egress of bile from the common duct; (2)

that it relaxes the sphincter of the common duct; (3) that it causes contractions of the gall-bladder reflexly; (4) that it excites the liver cells to a greater production of bile. According to the experimental work of Mendenhall, McClure and Cate (1926), the last-mentioned action is the one actually operative.

External Uses.—Magnesium oxide and the carbonate are used as a toilet powder, to dry the skin, to prevent chapping and excoriation in **intertrigo**, and to relieve the irritation due to **sunburn** and that left after shaving.

Magnesium sulphate was shown by H. Tucker to be of great value as an application in **local inflammatory conditions**. From 15 to 20 thicknesses of gauze, or a thin layer of absorbent cotton, should be placed as a covering over the entire inflamed area and kept continuously wet with a saturated solution of the salt, evaporation of which may be slowed by a final covering with oiled silk or waxed paper. The dressing is allowed to remain twelve to twenty-four hours, the parts being then washed with water and the dressing at once reapplied, if indicated. Pain is relieved and resolution of the inflammatory process hastened by this measure. A marked blanching of the affected surface is produced, but this is not followed by any deleterious effects. Tucker employed this procedure with marked success in cases of **gonorrheal epididymitis** and **orchitis**, **chancroidal bubo**, **gonorrheal arthritis**, **acute rheumatism**, **tuberculous peritonitis**, **facial erysipelas**, **cellulitis**, **alcoholic and traumatic neuritis**, **sprained ankles**, and **simple contusions**. Among others, Fifield has also seen excellent results follow magnesium sulphate

applications in **mastitis**, inflammatory conditions of the female genital organs, **boils**, and **carbuncles**. He prepares the solution by dissolving 2 pounds of magnesium sulphate in 1 gallon of hot water, and filtering when the solution has cooled. The applications of the solution should be continued until all signs of inflammation have disappeared, and, meanwhile, absolute rest for the inflamed part should have been procured. **Dermatitis** due to **poison ivy** is another condition in which magnesium sulphate solution has proven effective.

Application of magnesium sulphate solution was found useful by S. Solis-Cohen in **deep-seated pains**, acute or chronic, as in **thoracic aneurism**, **gastric ulcer** or **cancer**, **lymphatic leukemia**, **acute pericarditis**, **sciatica**, **headache** of unknown origin, and **chronic pleurisy**.

In **myalgia** and **lumbago** McCarty has had gratifying results by bathing the parts in a hot (110° F.) 1:16 solution of magnesium sulphate. The bath should last at least twenty minutes, the skin being meanwhile constantly wiped with a cloth, and the treatment should be repeated daily until the condition is cured. The same author recommends the use of compresses of a cold 1:16 solution in **tonsillitis** and even **pneumonia**.

Waterhouse makes the following suggestions as regards the local use of magnesium sulphate: (1) In a troublesome condition of the ankles in old people in which the skin assumes a hard, crusty condition, with a dusky red or purplish color and frequent cracking, smarting, bleeding, and ulcer formation, the local use of magnesium sulphate solution softens the skin, enhances the blood-supply, and

initiates granulation. (2) In **neuralgic conditions** application of magnesium sulphate solution along the course of the nerve involved will often relieve the pain in a few minutes. (3) In **malaria, typhoid fever, and measles** sponging the skin once or twice a day with magnesium sulphate solution is a useful measure. (4) Repeated applications of magnesium sulphate solution to **corneal scars** interfering with vision will usually remove the condition entirely in six months. (5) In parts of the country where **chigoes and fleas** are annoying, sponging with magnesium sulphate solution in the morning is an effectual preventive measure. (6) In **tooth-ache** plugging with cotton wet with magnesium sulphate solution is a useful procedure.

Mixture of saturated solution of magnesium sulphate and glycerin in equal proportions used for the cure of local infection in a series of 14 cases of **wounds** of various kinds, **infected blisters, felon, and cellulitis**. In the latter condition the arm was packed in the hot solution from fingers to shoulders. All the infections were quickly controlled. Freese (N. Y. Med. Jour., Feb. 14, 1914).

Twenty-eight cases of **carbuncle** successfully treated with a **magnesium sulphate paste**. Eleven ounces of carbolyzed or pure **glycerin** are placed in a hot mortar, 1½ pounds of **dried** magnesium sulphate added, and the whole slowly stirred and mixed with a warm pestle. The resulting cream is hygroscopic and liquefies on exposure to the air. The paste is spread thickly on a piece of sterile white lint large enough for the inflamed area, and is well covered with jaconet and cotton. A profuse discharge of serum follows, and the dressing is renewed in 12 to 24 hours. In a few days the central slough separates and a raw granulating surface is left, which is dressed with

the paste until all signs of sphacelating cellular tissue have disappeared. The cavity is then packed daily and the undermined edges supported with strips of sterile lint about 1½ inches wide, wrung loosely out of a saturated magnesium sulphate solution made by dissolving 40 ounces of the sulphate in 30 ounces of boiling water and 10 ounces of glycerin and sterilizing in an autoclave. This is covered with a double layer of lint saturated with the solution. This dressing is renewed daily until the healthy, firm granulation tissue is level with the surrounding skin margins. A. E. Morison (Brit. Med. Jour., Apr. 19, 1924).

In **tetanus** intraspinal injections of a 25 per cent. sterile magnesium sulphate solution have been productive of good results in a number of instances. The dose originally recommended by Meltzer was 1 c.c. (16 minims) of this solution for every 25 pounds of body weight. Since only a slight excess of magnesium solution is required to produce respiratory depression, complete relaxation with it should not be sought, but the spasms merely alleviated enough to prevent exhaustion.

C. E. DE M. SAJOUS

AND

L. T. DE M. SAJOUS,
Philadelphia.

MALARIAL FEVERS.—SYNONYMS.—Ague; intermittent and remittent fevers; chills and fever; quotidian, tertian, and quartan fevers; estivoautumnal fever; paludal fever; marsh fever; climatic fever; jungle fever; swamp fever; coast fever; mountain fever; hill fever; gnat fever; Roman fever; Chagres fever; Cameroon fever; chill fever; cold fever; hemamebiasis; paludism.

DEFINITION.—The term *malarial fevers* includes a group of closely allied infections characterized, as a rule, in

the acute forms, by periodic paroxysms having the three stages of chill, fever, and sweat. They are caused by the inoculation into the blood-stream, through the bite of a mosquito of the genus *Anopheles*, of certain specific protozoan parasites (*Hæmamaeba* [*Plasmodium*] *malariae* and its related species) which attack and destroy red blood-cells. Chronic hæmamebic infection manifests itself in various forms, and with its results is known as *chronic malaria* and *malarial cachexia*.

HISTORY.—The sober history of the development of our knowledge of the malarial fevers reads like a romantic fable wherein mighty giants of an hundred heads are met and conquered. Two of the giant-quellers (Laveran and Ross) were awarded the Nobel prize in medicine, and a third (Gorgas) was signally honored by the Congress of the United States as well as by American and foreign scientific associations.

Craig distinguishes four main epochs:

1. From the earliest records to the introduction of cinchona bark (1640).
2. From the introduction of cinchona bark to the discovery of the plasmodia (1882).
3. From the discovery of the plasmodia to the discovery of the method of transmission by the mosquito (1895).
4. From the discovery of the method of transmission until the present time.

The writers suggest that the fourth epoch should close with the achievements of Gorgas and his co-workers on the Isthmus of Panama, and would thus phrase its description: 4. From the discovery of *Anopheles* transmission to the banishment of malaria from the Panama Canal Zone and the completion of the canal. They would then add: 5. From the

completion of the Panama Canal (1914) on. For perhaps we are on the brink of other epoch-marking discoveries in regard to the malarial fevers.

GEOGRAPHICAL DISTRIBUTION.—With the exception of the Arctic and Antarctic regions, malaria, although principally a tropical disease, exists over the entire surface of the habitable globe.

North America.—From Canada to the Isthmus it is found, though relatively less common and less malignant in the north than in the south, in the highlands than in the lowlands, and virtually absent from the altitudes. All forms are encountered in the Mexican coast regions, as in the Gulf States of the Union, and along the Mississippi and Ohio Rivers. It is prevalent through the Middle West, but less so in the Middle States, if one excepts certain regions of New Jersey, Delaware, and Maryland. The World War caused a marked recrudescence of malaria in Europe, especially in Italy.

Malaria is still endemic in southern New England. It is 7 times as prevalent in rural districts as in urban, and is often benign, self-treated or self-limited. It is almost entirely of the tertian type. During the period of the War army, April, 1917, to Dec., 1919, there were 84 cases of malaria in the troops while in New England. M. J. Quinn (Boston Med. and Surg. Jour., Feb. 11, 1926).

Central and South America.—Here it is a veritable menace. Some regions are uninhabitable, owing to the virulence of the infection. The Panama Canal Zone is an exception only because of the vigilance of the United States Army Medical and Sanitary Corps.

West Indies.—In the Caribbean Islands malaria is very prevalent, and especially the malignant forms. Cuba and Porto Rico are both severely infected.

Europe.—Great Britain and Norway enjoy only a comparative freedom. Benign tertian exists on the Continent. Greece, Sicily, Italy, and Turkey are the worst sufferers, and exhibit also many cases of estivo-autumnal, even pernicious infection. Quartan infection is not rare in the Mediterranean countries.

Asia.—India harbors the disease in all its forms and degrees of severity. The annual loss of life here is tremendous. Japan and the Philippines have no exemption. In Syria and Mesopotamia the morbidity is large.

Africa and Oceanica.—Parts of Africa are uninhabitable owing to the ravages of the disease. This is especially so along the Congo and Nile Rivers. In Egypt, Tunis, Tripoli, and Algeria the infection exists endemically. It is prevalent in Australia, along the coast, and the same is true of the South Sea islands in general.

ECONOMIC LOSS.—Howard has estimated the loss in the United States due to malaria, calculating the loss in wages, lowered production, care of the sick, and medical attention as \$100,000,000 annually. India's toll of death is given at the startling, almost incredible figure of 1,130,000 souls yearly. Celli states that "malaria annually costs the Italian Government incalculable treasure."

These bare, indisputable facts place the problem of control and eradication squarely up to all governments.

CLASSIFICATION.—Acute malarial fevers were formerly classified according to clinical type as *intermittent* and *remittent*,

the former being subdivided into *quotidians*, *tertians*, and *quartans*, with the rare forms showing fortnightly (14 or 15 days) recurrence of paroxysms, sometimes distinguished by special title, as *quatuordecimam*, etc. The fulminant, specially virulent cases were, and still are, termed *pernicious malaria*. The term *malignant malaria*, formerly used synonymously with pernicious malaria, is now applied by some writers to all forms of infection with crescent-forming parasites, whether of the specially pernicious types or not—i.e., synonymously with *estivoautumnal infection*. The syndrome marked chiefly by splenic tumor and profound anemia resulting from long-standing infection, was designated *malarial cachexia*—a term still in reluctant use. Cases of malarial infection (most frequently *chronic*) not revealed by frank paroxysms of chill and fever, but manifesting other symptoms, such as headache, myalgia, neuralgia, paralyses, gastric and other visceral crises, etc., were known as *masked malaria*, or *larval malaria*. In popular parlance, the terms *brow ache*, *dumb ache*, *sun pain*, etc., were employed, and the enlarged spleen of chronic malarial infection was called "ague-cake."

At present most students of malaria adopt one or the other of two classifications based upon the type of the infecting organism,—(a) Mannaberg's and (b) Craig's modification of Schaudinn's.

Mannaberg's classification follows: 1. Fevers produced by Golgi's common tertian and quartan parasites. 2. Fevers produced by crescent-forming parasites. 3. Fevers produced by an association of both forms. 4. Latent infections.

Craig's classification, which in the main has been adopted in this article is the following: 1. Tertian malaria (*Plasmodium vivax*). 2. Quartan malaria (*Plasmodium malariae*). 3. Tertian estivoautumnal malaria (*Plasmodium falciparum*). 4. Quotidian estivoautumnal malaria (*Plasmodium quotidianum*).

We shall, however, use the term *hemameba* in preference to *plasmodium*, and shall take account, with Mannaberg, of *mixed infections* and, with traditional as well as modern medicine, of *latent* or *masked* infections. *Chronic infection* and its resultant *malarial cachexia* are likewise considered.

ETIOLOGY.—Methods of Infection.—Three main theories of the mechanism of malarial infection may be mentioned: 1. Through the digestive tract—water theory. 2. Through the respiratory tract—air theory. 3. The inoculation theory.

Although the air and water theories still have a few adherents, the available evidence against them is so overwhelming that they may be dismissed from consideration. The present status of the question is well summarized by Bignami: "This much at any rate we can assert, namely, that inoculation is the only mechanism of infection which has been demonstrated experimentally."

Predisposing Factors.

These may be considered under two heads—environmental and individual.

A. Environmental.—1. *Climate.*—Malarial fevers are more prevalent and more virulent in hot and damp climates, especially tropical and subtropical countries in which there are extensive swamps and jungles—conditions which favor the propagation of mosquitoes and probably affect also the intensity of the life of the malarial parasites. The infections of the temperate zones are more commonly benign. Malarial fevers are found wherever conditions favor the life of the mosquito. In Philadelphia, "the Neck," a region of marshy truck farms, was long the habitat of the disease, while residents of the built-up districts suffered chiefly when the streets were torn up—and especially after spring and summer rains. In any climate infested by mosquitoes of the genus *Anopheles*, and in which infected human beings live, malaria will persist, and must be repressed by public and private precautions.

It has been found that the malarial parasite will not develop with a mean temperature below 60° F. As great altitudes are for the most part cool and dry, afford better drainage, and in consequence are poor breeding places for both parasite and insect, it is easily seen why marshy lowlands suffer most. Exceptions to this are found in the Philippines and in South America.

2. *Rain and Moisture—Soil.*—Rain and moisture furnish the best conditions for the development of breeding places, and the soil which favors the formation of stagnant pools is like a virulent focus for infection. These conditions are found in forests and swamp lands, and in soil which does not admit of free drainage.

3. *Season.*—The influence of season is shown in the following tables, compiled by Thayer, of Baltimore; the Isthmian Canal Commission, and Celli, as regards their respective countries and climates. It will be seen that the greatest number of cases occur in summer and early fall. The estivoautumnal types reach their height in the autumn in the tropics, and during late summer in temperate climates, while the simple tertian variety is most common during the summer.

B. Individual Causes.—1. *Race.*—It is said that dark-skinned races are less susceptible, partly by natural resistance and partly owing to an immunity gained by repeated infections during childhood. New arrivals in malarial districts are more susceptible than older inhabitants, especially if they belong to light-skinned races.

2. *Sex and Age.*—As a rule, men are the most exposed. When both sexes are equally exposed the ratio of infec-

TABLE 1.—CELLI'S TABLE: SEASONAL VARIATION IN ITALY.

Months	Years													Total
	1864	1865	1873	1874	1877	1878	1892	1893	1894	1895	1896	1897	1898	
January	284	195	853	459	638	661	240	189	249	236	314	129	90	4673
February ...	228	198	681	528	519	543	177	125	163	175	243	94	58	3732
March	189	170	711	747	544	502	231	119	125	165	244	98	61	3906
April	168	151	658	675	564	576	223	148	157	180	235	115	76	3921
May	112	114	669	584	480	504	244	119	159	165	229	120	76	2575
June	83	88	409	331	339	375	205	119	138	150	155	88	73	2553
July	439	340	1135	865	1858	398	608	553	813	582	502	320	431	8844
August	1492	570	2824	2647	2373	1604	694	741	1298	1181	939	410	905	17678
September .	1056	476	2185	2019	1995	1896	586	761	984	1357	684	505	799	15203
October	775	437	1761	1732	1460	1495	500	911	855	1191	532	403	708	12755
November ..	431	475	1280	1186	795	1245	404	831	678	898	361	215	732	9531
December ..	271	205	777	778	695	1193	311	427	427	767	252	137	386	6621
Total	5528	3419	13938	12682	12260	10992	4423	5043	6046	6947	4690	2634	4390	92992

TABLE 2.—THAYER'S TABLE: SEASONAL VARIATION IN BALTIMORE.

Type	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sep.	Oct.	Nov.	Dec.
Tertian	12	12	28	51	76	68	131	161	153	168	54	17
Quartan	3	1	0	1	0	0	3	0	2	1	4	2
Estivoautumnal.	5	1	2	5	0	3	37	99	191	203	63	22
Combined	0	1	1	0	0	1	3	3	4	11	6	2
Total	20	15	31	57	76	72	174	263	350	383	127	43

TABLE 3.—ISTHMIAN CANAL COMMISSION, 1911.

Months	Discharged		Died		Total Cases	Annual Average per 1000 of deaths	Annual Average per 1000 of cases	Number of Employees
	W.	C.	W.	C.				
January	180	157	1	1	339	0.51	86	47,348
February	217	156	1	..	384	0.24	93	49,785
March	239	167	..	1	407	0.25	102	47,935
April	190	138	1	..	329	0.25	81	48,634
May	461	463	1	3	928	0.99	230	48,496
June	756	981	4	4	1745	1.98	432	48,519
July	747	1226	4	4	1981	2.01	497	47,801
August	396	506	3	2	907	1.21	219	49,710
September	322	339	3	..	664	0.76	168	47,400
October	253	249	1	..	503	0.24	121	49,812
November	199	210	4	1	414	1.19	99	50,420
December	191	193	1	1	386	0.47	91	50,655
Total	4151	4795	24	17	8987	0.84	184	48,876

tion is the same. Children are less resistant to infection than adults.

Malarial infection is less frequent in the infant than in the child or adult. Malaria, in the infant, is a serious disease, and demands prompt recognition and treatment. A positive diagnosis can not be made ex-

cept by repeated blood examination. Therapeutic diagnosis should not be made unless it is impossible to make a diagnosis by blood examination. The treatment of malaria in the infant is as in the adult. Morgan Smith (Trans. So. Med. Assoc.; N. Y. Med. Jour., Jan. 19, 1918).

Substances causing the spleen to contract (adrenalin, ergot, hypophysis) can cause the contained parasites to enter the circulation. Neuschlotz (Münch. med. Woch., Jan. 22, 1918).

The repeated subinoculation of malarial blood from man to man through more than 20 passages in no way alters the virulence or virility of the parasites, nor does the disease thus produced differ in any remarkable degree from that acquired through the bite of infected anopheline mosquitoes. Editorial (Lancet, May 24, 1924).

3. *Occupation*.—Laborers upon the soil, ditch diggers, railroad builders, etc., especially where through great enterprises the soil is turned and returned, favoring the formation of stagnant pools, are especially liable—the more so in highly malarious districts—to infection. Morbidity is increased where night work is required. In a less degree, but according to the extent of their exposure, engineers, contractors, supervisors, and other officials engaged in railroad and canal construction, etc., are similarly liable. Soldiers in camp or “on the hike” in malarial countries and climates suffer largely.

4. *Social and Hygienic Conditions*.—Poorly nourished individuals, dwellers in insanitary abodes, and those who are careless of their personal hygiene or of prophylaxis—as in sleeping near the ground without protection—often succumb to the infection. Especially is this true of the laboring and peasant classes and of soldiers.

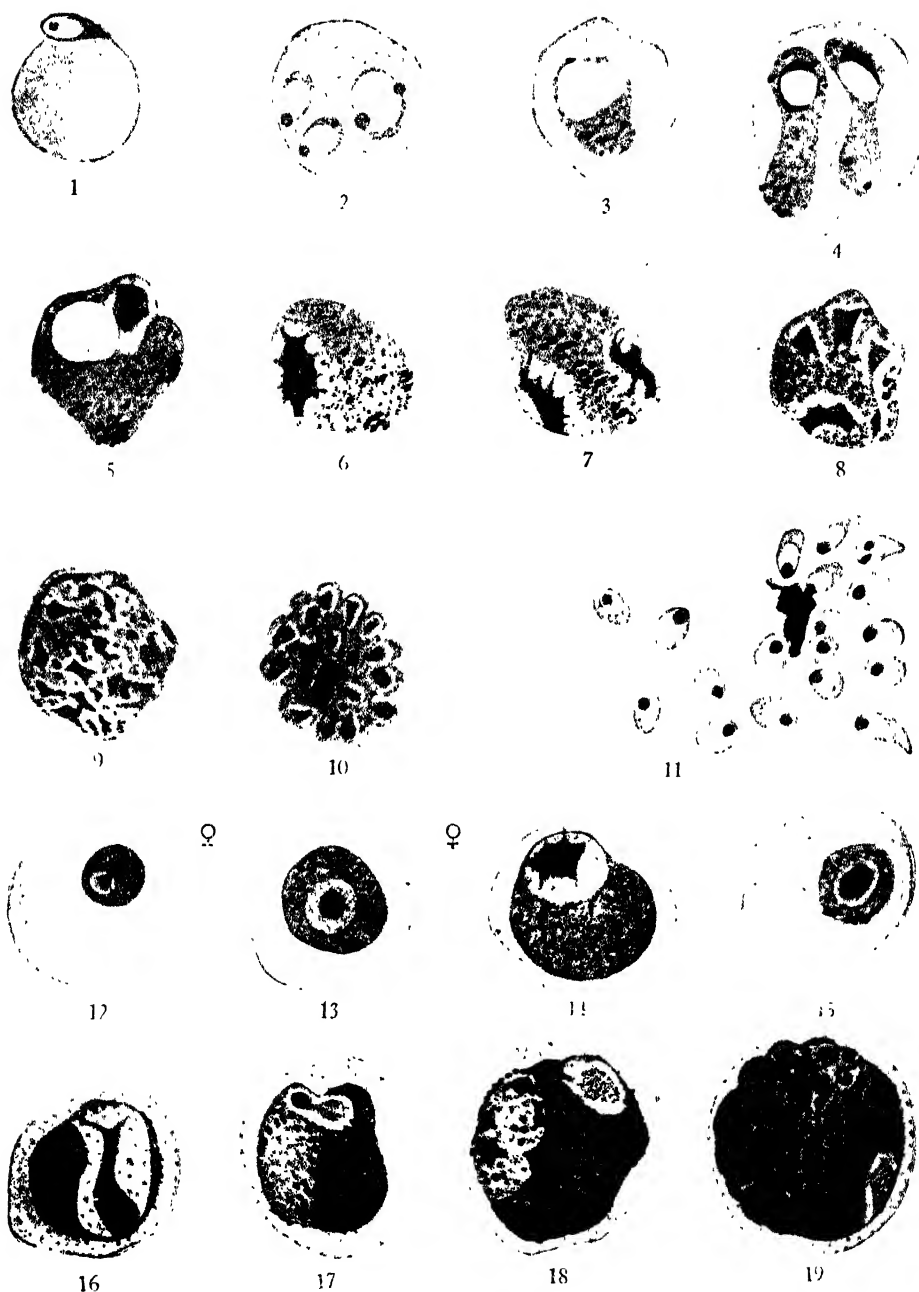
Parasitology.—The parasites of malaria (malarial organisms, malarial corpuscles, plasmodia, hemamebæ), discovered by Laveran in 1882, have two cycles of development—one within certain mosquitoes of the genus *Anopheles*; one within man.

The *mosquito cycle* is sexual (*sporogony*); the *human cycle*, for the most part, asexual (*schizogony*). Whether or not the parasites have, in the present stage of evolution, a third, non-parasitic stage of existence is mooted, but there is no evidence of such. Bass has succeeded in cultivating them *in vitro*, but only within the red blood-cells of man. Apparently they are transferred from insect host to human host, and back again to new insects, new men, continuously. Hence malarial fevers, while dangerously transmissible, are not contagious; i.e., they are not directly infectious from patient to patient.

In man the parasites chiefly inhabit the blood-stream, living on and within the red corpuscles, by destroying which they produce anemia and the peculiar pigmentation of malaria. They can sometimes be demonstrated during life in blood taken from the spleen, when examination of the peripheral blood fails to reveal them. *Post mortem* they have been found within the blood-vessels of all the organs and tissues.

Several species, types, and varieties of malarial organisms are recognized and have received distinctive names. Of these, sharp distinction may be made between two groups, the *crescent-forming* and *non-crescent-forming* hemamebæ. The former, highly resistant and dangerous, give rise to the so-called *malignant* or *estivoautumnal* infections, while the latter cause the comparatively mild and manageable *ordinary* infections.

The non-crescent-forming organisms are commonly spoken of as (*ordinary*) *tertian* and *quartan* parasites, from the periodicity (about forty-eight hours and about seventy-two hours, respect-



TERTIAN MALARIAL PARASITE (*Plasmodium vivax*) (Billet. Traité du Sang of Gilbert and Wenberg.)

1 to 11, asexual forms. 1, normal red cell with microzoite about to enter, 2 and 3, early ring forms; 4, pigmented hemogregarinoid form, 5, adult schizont, 6 to 10, segmentation; 11, liberation of merozoites. 12 to 19, sexual forms. 12 to 14, development of macrogamete or female gamete; 15 and 16, development of microgametocyte or male cell; 17 to 19, parthenogenesis in a macrogamete

ively) of the paroxysms that they excite. The crescent-forming organisms are commonly spoken of as *estivo-autumnal* parasites, from the season of the year (summer and autumn—i.e., the *hot months*) in which the fevers they originate are most frequently met with. They are of two varieties, *quotidian* and *tertian*, showing a periodicity, respectively, of about twenty-four hours and about forty-eight hours.

Non-crescent-forming Organisms.—The *tertian* parasites, *Hamamaba* (or *Plasmodium*) *vivax*, in their human cycle (*schizogony*), appear first within the red blood-cells, as small, actively ameboid, hyaline bodies—the *schizonts*. These are of various shapes, their outlines changing with their ameboid movements. In this *hyaline stage* the organism is ill defined, and can be discerned only by very careful examination. A few minute, reddish-brown granules appear within it—pigment elaborated by the organism from the hemoglobin of the invaded red cell. The pigment granules show a constant and rapid movement, which is, however, passive, not active, and is the result of protoplasmic flow within the parasite. At first the schizont occupies but a small portion of the infected cell, but in its progress to maturity it gradually encroaches more and more upon the substance of the latter, until at the end of about thirty-six hours there is left but a narrow and much dilated rim of cell substance inclosing the almost full grown organism. This has a well-defined circular outline. Ameboid motion has become almost entirely lost, but the pigment, which is much increased in quantity, is still granular and more or less motile. The diameter of the ring of eryth-

rocyte substance inclosing the *adult parasite* is much increased—nearly double that of the normal corpuscle. Toward the end of from forty-five to forty-eight hours, *segmentation* of the parasite takes place. The pigment begins to clump in the center or at one side of the organism, and the *rosette stage* is formed. Fine radial divisions branch out from the center toward the periphery, dividing the parasite into small ovoid sections (or segments) known as *merozoites*. These vary in number from 12 to 24, the average being about 16. Generally they are arranged in two rows, one row about the center of the organism and the other peripherally to this; but irregular arrangement is not rare. The merozoites are always free from pigment. The rosettes now undergo complete division, each merozoite becoming a separate living entity.

The infected red cell has by this time apparently disappeared. Its destruction by absorption or rupture liberates the rosettes or the separated merozoites, which last, infecting new erythrocytes, again appear as schizonts. The life-cycle within man thus continues.

The process of segmentation and division is termed *sporulation*, and its acme coincides with the clinical paroxysm. It is at this stage that parasitocides, especially quinine, are most effective. Indeed, it has been shown that the blood-serum alone destroys many of the merozoites, and others, even the undivided rosettes, are engulfed by the phagocytes. Phagocytosis of red cells containing dead parasites also takes place. According to Bass, but 1 segment in 15 or 30 survives to infect new red

corpuscles. This observer indeed, basing his opinion upon his ingenious culture experiments, asserts that the young parasites cannot exist free in the blood. He believes that they must pass directly from infected to uninfected cells, where the erythrocytes are crowded together in the capillaries, and this only when the opening for the exit of merozoites from the red cell is toward another in contact with it. If the opening in the infected cell occurs on the side in the direction of the blood-current, the merozoites are killed at once.

A certain proportion of the adult parasites, however, do not segment, but become flagellated. These are the *gametes* or sexual forms, which are destined to carry on the life cycle of the organism in the mosquito—*sporogony*. They have been observed chiefly in blood which has been for some time (eight or ten minutes) removed from the body, and were thus first demonstrated; but it is now known, as predicted by the senior writer, that a certain number of sexual parasites are formed within the human vessels, probably in the deeper and less active portions of the circulation, and it is possibly thus that chronic and larval infections are maintained.

The flagellated organisms are of two kinds, designated by Craig as *active* and *passive*. The active flagellated organism, also termed the *microgametocyte*, is at first a spherical body filled with motile pigment, distributed throughout the protoplasm in the form of small granules. The motion of these granules becomes more and more rapid, indicative of greater and greater activity of the protoplasm, until finally, at the cir-

cumference of the organism, 3 or more thread-like and wavy prolongations (flagella) are put forth, which may be in length from 3 to 4 times the diameter of the parasite. They exhibit active lashing movements, and when separated from the main body of the parasitic cell are known as *microgametes*. Roughly, they correspond to the spermatozoa of higher animal forms.

The passive flagellated organism, or *macrogamete*, is a round body containing pigment in larger, immotile clumps, generally arranged in ring form around the periphery. These bodies do not of themselves produce flagella, but upon the slide, in drawn blood, flagella from the microgametocytes which have become free in the plasma can sometimes be seen attached to the macrogametes.

In nature it is in the stomach or middle intestine of the mosquito that the conjunction of male and female elements—of micro- and macrogametes—takes place. The fertilized female cell is known as the *sporont*. It becomes elongated and finally motile, and is then known as the *ookinete*. The ookinete penetrates the wall of the middle intestine and attaches itself to the basement membrane of the intestine, on the lower side of the epithelium, between the adipose tissue and the muscular wall. Here it becomes spherical in shape, forming the *oocyst*, about the third or fourth day after the mosquito has bitten an infected individual. The protoplasm of this cyst is granular and reticular in appearance; the pigment is reduced in amount, and the whole is inclosed within a well-defined capsule. About the fifth or sixth day the oocyst enlarges and



QUARTAN MALARIAL PARASITE (*Plasmodium malarium*) (Billet - *Traité du Sang* of Gilbert and Wernberg)

1 to 17. Asexual forms. 1, red cell containing ring form; 2, ricket form; 3, bacilloid form; 4, pyriform form; 5 to 8, pigmented hemogregarinoid forms; 9, band form; 10, adult schizont; 10 to 17, sexual maturation. 18, macrogamete; 19, microgametocyte; 20, parthenogenesis in a macrogamete.

within it are formed spherical, refractive bodies known as *sporoblasts*, which in the course of a week or so develop into a large number of delicate filaments having pointed extremities and containing a small amount of chromatin. These are the *sporozoites*. Liberated by the rupture of the cyst, the sporozoites migrate through the tubules of the salivary glands of their insect host, and the infected mosquito, when it bites a human, inoculates them into the blood-stream. Penetrating the red cells, they appear as faintly refractive bodies, develop, and finally divide into merozoites, and complete the human cycle of the parasite. The entire cycle of the parasite in the mosquito is completed in about ten days.

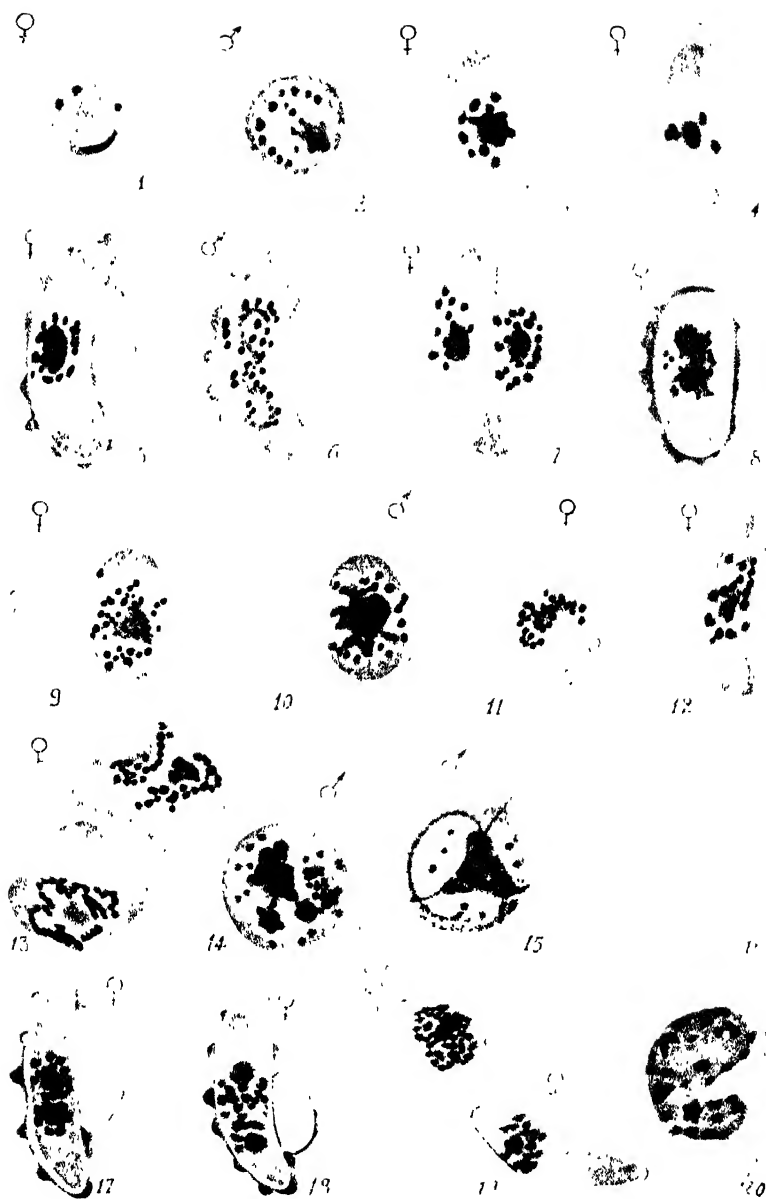
Like the tertian parasite, the *human malaria* is a malarial infection (*Human malaria*). It is first within the human red blood cell, where it develops as a merozoite body, and then in the blood-schizont. The merozoite body is marked by a distinct outline, and is re-organism. It is not, however, as demented, that the merozoite body is darker, and the merozoite body is around the merozoite body. The organism is distinct in outline, and the merozoite body is distinct in outline. The merozoite body is fever does not tend to be less than that in the merozoite body. The merozoite body is color. The merozoite body is distinguishing the merozoite body upon a microscope. The parasite is ing at the same time. The pigment in the merozoite body is

and, collecting at the extreme periphery of the organism, becomes absolutely immotile.

The parasite tends more and more to fill the infected erythrocyte, and when it is full grown there is visible but a small greenish rim of hemoglobin around the periphery. The plasmodium is now distinctly outlined, being much more refractive than the tertian organism. At the end of about twenty-two hours, segmentation occurs, the pigment collecting in a star-like form. Radial striations appear, dividing the organism into from 12 to 16 merozoites, which, as a rule, are arranged in a perfectly symmetrical manner around the central pigment, giving rise to the so-called "star-like" form of the merozoite.

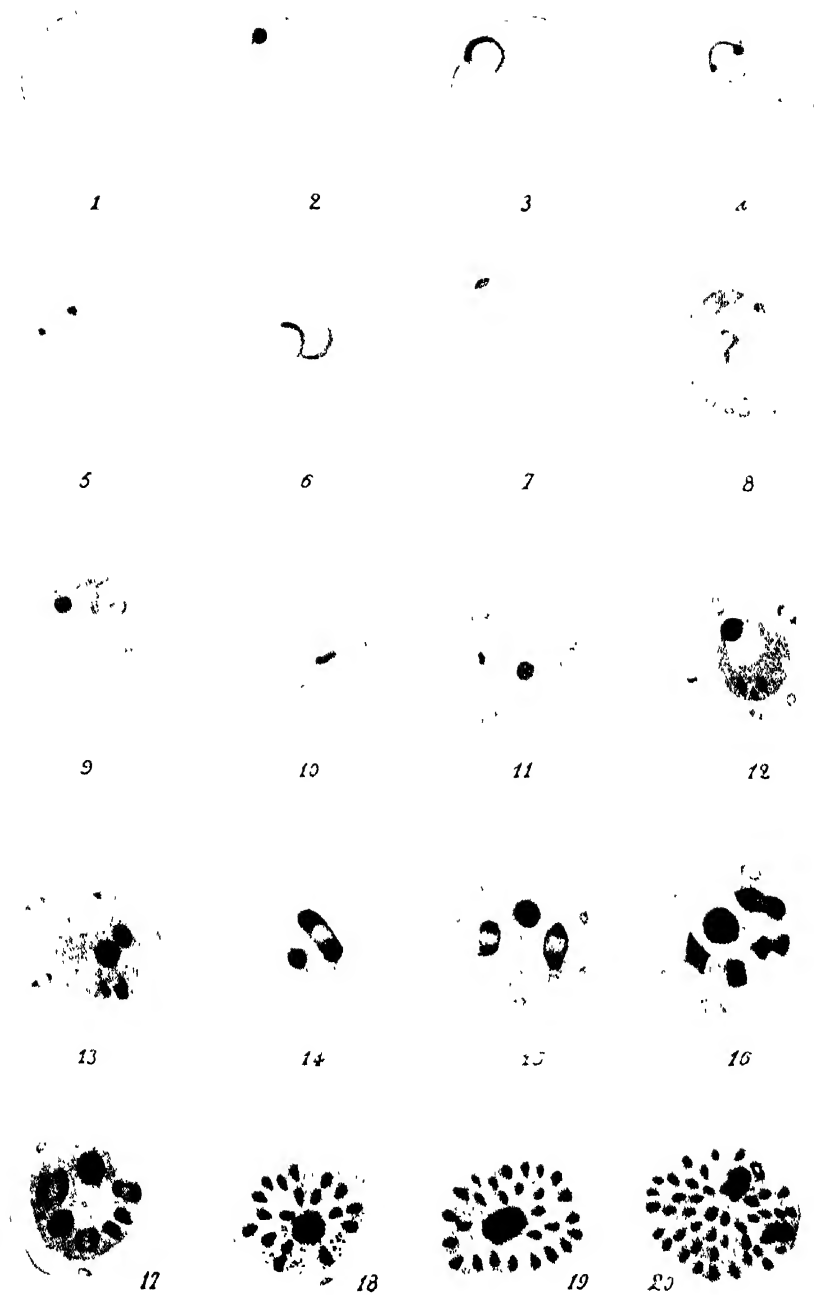
The infected red cell ruptures or dissolves, and the merozoites divide of the merozoite body. The merozoite body is in the blood-schizont. The merozoite body is in the human life-cycle, marked by a distinct outline, and is re-organism. It is not, however, as demented, that the merozoite body is darker, and the merozoite body is around the merozoite body. The organism is distinct in outline, and the merozoite body is distinct in outline. The merozoite body is fever does not tend to be less than that in the merozoite body. The merozoite body is color. The merozoite body is distinguishing the merozoite body upon a microscope. The parasite is ing at the same time. The pigment in the merozoite body is

and the tertian. The merozoite body is in the human life-cycle, marked by a distinct outline, and is re-organism. It is not, however, as demented, that the merozoite body is darker, and the merozoite body is around the merozoite body. The organism is distinct in outline, and the merozoite body is distinct in outline. The merozoite body is fever does not tend to be less than that in the merozoite body. The merozoite body is color. The merozoite body is distinguishing the merozoite body upon a microscope. The parasite is ing at the same time. The pigment in the merozoite body is



P. FALCIPARUM J. MALAKI. PARASITE (*Plasmodium falciparum* Sexual forms—Female gametes or macrogametes, male gametes or microgametocytes, Parthenogenesis). (*Bullet. Traité du Sang* of Gilbert and Wernberg.)

1 to 7, intracorporeal cycle of the gametes. 1, young female gamete; 2, young male gamete; 3 and 4, older female gametes; 5, adult female gamete (crescent); 6, adult male gamete (crescent); 7, two macrogametes in a single red cell. 8 to 12, extracorporeal cycle of the gametes. 8 to 12, loss of the cell capsule; 13, motile, ameboid macrogametes; 14, non-motile microgametocyte; 15, extrusion of flagella or microgametes by microgametocyte; 16, flagella; 17 to 20, parthenogenesis in a macrogamete.



ESTIVOAUTUMNAL MALARIAN PARASITE (*Plasmodium falciparum*, Asexual Forms). (*Billet: Traité du Sang* of Gilbert and Weubere.)

1, normal red cell, 2 to 6, ring forms, 7 to 10, entrance of parasite more deeply into the red cell; 10 to 20, intracorpuseular forms, 13, adult schizont; 14 to 20, segmenting forms (schizogony).

shorter and plumper than in the tertian. Its extremities are rounded, and it always presents a distinct double outline. The protoplasm is less granular and the pigment is smaller in amount, and in the form of dots.

In the mosquito (and upon the slide in the blood which has been drawn for some time) the crescents undergo a series of changes, first becoming oval and then round. These spherical bodies correspond to the *microgametocytes* and *macrogametes* of the tertian and quartan infections, and in the mosquito undergo similar changes. The *microgametocytes* become flagellated; the male elements (flagella, or *microgametes*) become free and fertilize the female elements (*macrogametes*); the *sporont*, the *ookinete*, the *oöcyte*, the *sporoblasts*, and finally the *sporozoites* develop, and the latter, entering the proboscis of the mosquito, are again inoculated into human beings.

Like the quotidian, the tertian estivoautumnal parasite—*Hamamaba* (or *Plasmodium*) *falciparum* (tertianum)—in its schizogony, or human cycle, appears first within the infected red cell as a hyaline ring or disk. The infected corpuscle is greenish in color, smaller than the normal corpuscles, and generally crested. The young parasites are considerably larger than the corresponding forms of the quotidian organism, occupying from one-third to one-half of the area of the infected red cell. The ring forms are smaller in outline, one portion being larger than the rest, giving the so-called "signet-ring" appearance. The organism is highly refractive, and sharply defined, as with a punch. Rarely does it show a single nucleus and within the

puscle. Ameboid motion is less rapid than in the quotidian form, and as growth increases it becomes lost. The ring shape alters to the rounded form, and when full grown the organism occupies about one-half of the infected red cell. In the course of from twenty to twenty-four hours the hyaline forms exhibit fine, reddish-brown granules resembling those found in the quartan parasite. The pigment is generally motile. Segmentation occurs in from forty-five to forty-eight hours. The pigment collects at the center and radial striations starting from this point divide the parasite ordinarily into from 10 to 15 merozoites, although as many as 24 segments have been counted in some instances. Division of the rosette occurs within the red cells. The segmenting forms, however, are seldom found in the peripheral blood, although frequently very numerous in blood collected from the spleen. The merozoite segments liberated in the blood-plasma again infect the red cells, and thus the cycle is repeated.

The crescent of the tertian estivoautumnal infections is much more slender than that of the quotidian form, and has pointed extremities. It seldom shows a double outline. The protoplasm is finely granular and the pigment is large in amount and in the form of slender rods. The sporogony (mosquito cycle), is like that of the quotidian organism.

Crescents are produced from the ordinary asexual spores of *P. falciparum*, leading to a development of immaturity toward the latter. They develop somewhere in the internal organs and then appear suddenly in the peripheral blood. The period required for their development is about ten days. Crescents do not generally

live more than a few days in the peripheral blood. Fresh broods of them appear daily. Thomson (Annals of Trop. Med. and Parasitol., Apr., 1911).

Intracorpuseular Conjugation.—It is difficult to account for some of the cases of long-continued, latent, masked, and recurrent infections—especially those of semiannual and annual recurrence over long periods of years, as described by the senior writer—without reinfection. We are inclined to believe with Celli that there is a highly resistant resting or larval form of the parasite, which takes refuge in the deeper tissues, spleen, or bone-marrow, and under certain conditions reproduces and again invades the peripheral bloodstream. We are of opinion from our clinical studies that the irritation of a relatively small dose of quinine may be one of these conditions. Archibald Billings early in the nineteenth century observed masked malaria pass into frank ague when the patient was removed from the sea level to altitude, or from an ague-stricken to a free locality, or when a relatively small dose of cinchona was given. Craig has observed a phenomenon which he thinks throws light on the subject—the conjugation of two young hyaline ring forms within the red cell, and before the formation of pigment. He believes that this is absolutely necessary to the continuance of malarial infection in man, and that in cases in which it does not occur the organisms undergo asexual sporulation for a time and then perish—this leading to spontaneous recovery. He has observed conjugation most frequently in cases presenting severe symptoms. It occurs with all varieties of organisms, though most readily demonstrated in estivoautumnal infection. It has three stages, termed by Craig

(1) protoplasmic union; (2) complete protoplasmic amalgamation; (3) chromatic union. The spherical pigmented organism thus formed is liberated, and Craig believes that it may become encysted and thus enter upon a resting or *zygote* stage. Young organisms—spores—develop within it, and when released (after a long or short period) enter the red cells, initiating a new schizogony.

Cultivation of the Malarial Parasites.—C. C. Bass succeeded in cultivating the malarial parasites *in vitro*. To every 10 c.c. of defibrinated malarial blood is added 0.1 c.c. of 50 per cent. dextrose solution; the leucocytes are brought to the surface of the cellular deposit by centrifugation; the serum is placed in flat culture tubes to a depth of 12 to 25 mm., and 0.1 to 0.2 c.c. of erythrocytes from the middle of the cell deposit is placed in each tube. The tubes are then incubated at 40 to 41° C.

Malarial Mosquitoes.—Only one genus, so far as is known, is capable of propagating malaria—the *Anopheles*.

In North America 2 species of the *Anopheles* group of the *Anopheles* genus (*A. quadrimaculata* and *maculipennis*) are the principal malaria carriers, with species of the *Patagiamyia* group (*A. punctipennis*, *pseudopunctipennis* and *crucians*) playing a very subordinate part. In Central and South America, the principal carriers belong to the *Nyssorhynchus* group (*A. albimanus*, *argyritarsis* and *tarsimaculata*). F. M. Root (Proc. Internat. Conf. on Health Probl. in Trop. Amer., 1924).

Of the 50 or more known species of *Anopheles*, the following, according to Craig, have been shown experimentally to transmit the disease:

In Africa—*A. costalis*; *A. paludis*; *A. funesta*.

In India—*A. rossii*; *A. culicifacies*; *A. theobaldi*; *A. barbirostris*.

In Europe—*A. superpictus*; *A. maculipennis*; *A. bifurcatus*.

America—*A. maculipennis* or *punctipennis*; *A. argyrotarsis*; *A. crucians*.

Immunity.—The pigmented races appear to enjoy a relative immunity to malaria, which increases with the density of the pigment and is greatest (a) in the natives of malarial regions, and (b) in the most vigorous individuals. American negroes from non-malarious districts may become infected upon change of residence, although apparently less liable to infection than Caucasians, and although the negroes of the Gulf States and the West Indies do exhibit a high degree of immunity. It is probable, therefore, that a certain resistance is acquired as a result of repeated infections in childhood. The greatest prevalence of this immunity is found in East Africa; it is less in West Africa, and still less among the brown races in the Philippines. On the other hand, it is not observed among Italians in Italy or elsewhere. Kelch and Kiener, indeed, deny that any Europeans gain immunity, either by repeated infections or by acclimatization. They admit, however, a "relative tolerance" or a "diminished reaction." To this Mannaberg agrees, but also states that immunization does occur among East Africans, East Indians, Arabs, and Chinese.

SYMPTOMS AND CLINICAL COURSE.—**Period of Incubation.**—No fixed period of incubation has been determined. It varies between six and fourteen days, depending upon the type, virulence, and number of the infecting parasites. Mannaberg's inoculation experiments gave these results:—

Tertian: 7 cases, minimum six days, maximum twenty-one days, mean eleven days.

Quartan: 5 cases, minimum eleven

days, maximum eighteen days, mean thirteen days.

Estivoautumnal: 7 cases with hema-mebe without crescents, minimum three days, maximum fourteen days, mean six and five-tenths days; 2 cases with crescents, thirteen and fifteen days.

These experiments accord with what is known clinically, viz., that the milder the infection, the longer the incubation period. They may be compared with the senior writer's demonstration of the *freedom periods* following the subcutaneous injection of a single dose of 15 grains (1 Gm.) of quinine and urea hydrochloride. These were found to divide into two groups, irrespective of organisms, averaging in double tertians and tertians six and one-half and thirteen days, respectively. In one quartan case it was twelve and three-eighths days. It was observed, however, that organisms were present in diminishing number for three days after the injection, and reappeared and began to multiply about three days before the postponed paroxysm.

Symptomatology.

Simple Tertian Malarial Fever (*Hamamaba vivax*).—This is the most common and mildest form of infection met with in temperate climates. The paroxysms occur every forty-five to forty-eight hours, with the sporulation of a single group of parasites, each member being in approximately the same stage of development. Daily paroxysms (*double tertian*) indicate a double infection, with two groups of parasites. The interval between daily paroxysms is rarely an exact period of twenty-four hours. In many instances observed by the senior writer it was alternately twenty-one hours and twenty-four hours—thus indicating

forty-five hours as the time of ripening of each group. Sometimes it is (approximately) twenty-three hours, the paroxysms, as it is said, "advancing an hour" each day—again indicating a period of forty-five or forty-six, rather than forty-eight, hours.

The *paroxysm*, when typical, is divided into chill, fever, and sweating stages.

The *chill* is usually preceded by certain *prodromes*—headache, nausea, aching of the back and extremities, and a general sense of malaise or discomfort. As a rule, the onset is gradual. Chilly sensations are experienced in the feet (sometimes in the upper extremities) and spread upward along the thighs and spine, until, with the fully developed rigor, the teeth chatter and the body shakes violently. The face and lips become cyanotic, the skin of the trunk and extremities presenting the "goose-flesh" appearance (*pilomotor reflex*). Nausea increases, and vertigo and dimness of vision may develop; sometimes there is vomiting. The pulse is hard, rapid, and irregular. Although the patient complains of intense cold, asking for more bedcovers, and the surface of the body is cool, the thermometer shows an elevation of internal temperature, which (taken in the rectum) may reach 105° or 106° F. Large quantities of pale urine of low specific gravity may be passed during the chill, but, as a rule, this is a later phenomenon. The cold stage ordinarily lasts from ten or fifteen to thirty minutes, but may continue for an hour or longer in severe cases.

Gradually superseding the chill comes the *febrile stage*. The body temperature, which continues to rise, begins to impress itself upon the subjectivity. Warm flushes succeed the cold sensa-

tions, until the latter are lost and the patient throws off his bedclothing, complaining of the intense heat.

The skin becomes hot, dry, and reddened. The conjunctivæ are injected. The pulse becomes rapid, full, and bounding and the respiration hurried. Throbbing headache, tinnitus aurium, and delirium are sometimes present in severe cases, or the patient may become drowsy and sink into a semicomatose or comatose condition. Constipation is the rule, diarrhea occasional. Herpetic eruptions, erythema, and urticaria are not uncommon at the height of the febrile stage. Epistaxis is less frequent. In some cases petechiæ and even purpuric spots are seen. Enlargement of the spleen may ordinarily be detected. The duration varies from four to six hours.

As the fever declines, *sweating* begins. Great relief is often expressed by the patient, from the coincident amelioration of the distressing symptoms. Commencing over the face, the moisture rapidly spreads until the entire body is bathed in a profuse perspiration. The temperature rapidly declines, becoming subnormal within two or three hours. Weakness of the circulation may now be manifested. The pulse and respiration lessen in frequency, and the patient falls into a refreshing slumber.

In children under 4 or 5 years the chill may be absent or pass unnoticed; but there is vomiting, sometimes profuse and persistent. The child is pale, sleepy, and prostrated, with lips and finger-tips blue, and the face is often anxious and drawn. Rapid rise of temperature to 104° or 105° F. (40° to 40.5° C.) follows, fever lasting three or four to ten or twelve hours. The subsequent sweating is not nearly so marked as in adults; it is sometimes apparently absent alto-

gether. The intervals between paroxysms are not always regular. Enlargement of spleen is usually present if the case has progressed without treatment. In irregular types of malaria in children, the most distinctive signs, outside of positive blood examination, are the periodicity of the temperature and the fact that the child seldom seems as ill as would be expected from the high temperature. Wherry (Archives of Pediat., Apr., 1911).

In infancy, up to 3 years, the fever was found to be often remittent, irregularly intermittent, or absent, and enlarged spleen was lacking in fully 30 per cent. of cases. Chills were absent. Breast-fed children grew indifferent to nursing, stopped gaining weight or lost, and became anemic. Vomiting was present in 75 and mild diarrhea in 25 per cent. Tetany, asthma, or bronchitis were sometimes precipitated by a malarial attack. W. A. and F. X. Mulherin (Jour. Amer. Med. Assoc., June 17, 1922).

Unusual case of malaria showing sudden unconsciousness and convulsions as first symptoms, with absence of fever and of enlarged spleen at the start. Fever followed, but for one day only. Consciousness returned after the first dose of quinine, given intravenously. Parasites continued present in the blood even after 8 days' quinine treatment. N. Ghosh (Indian Med. Gaz., Dec., 1925).

During the *intermission* which now occurs, the patient may feel perfectly well, but if treatment has not been instituted the paroxysm recurs at the appointed time (coinciding with the sporulation of the new brood of parasites) and follows the same course as before.

Double Tertian Infections.—Within the blood will be found two different groups of organisms reaching maturity on alternate days, thus giving rise to daily paroxysms. The relative intensity of the respective paroxysms will

depend upon the relative number in, and virulence of, the infecting groups. Sometimes one group is so much less numerous or less active than the other that the paroxysms remain tertian for some time, becoming of daily occurrence only when the second group of parasites has multiplied sufficiently.

Multiple tertian infection gives rise to a *remittent* or *subcontinuous* type of fever. As the various groups of organisms mature at different times, there is neither an evident periodicity nor a complete intermission during which temperature remains normal and the patient feels well; nor, after the first (or first few) paroxysms, is there likely to be distinctive repetition of the three stages of chill, fever, and sweat. "Remittent fever" is not so frequently described at the present time as a generation ago, nor is it so commonly met with in Philadelphia (we cannot speak for other localities).

Doubtless some of the cases that have been called "remittent malaria" were really typhoid fever—but not all of them. This form of fever is much more common and important in estivo-autumnal infections than in non-crescentic types.

Quartan Malarial Fever (*Hæmamba malarie*).—This is the rarest type of malarial infection. Craig observed only 26 instances in 5000 cases. The only undoubted cases (4 in number) seen by the writers (in Philadelphia) were in the persons of Italians, or of sailors from West Indian or South American ports.

In uncomplicated quartan infections, the paroxysms recur in about seventy-two hours, being coincident with the recurrent sporulations of a single group of parasites of approximately the same stage of development. The *symptoms*

are like those of tertian infections, but, as a rule, more severe. The combined duration of the chill, fever, and sweat is about twelve hours.

Cases of double infection have one free day between two paroxysm days in each seventy-two hours. In triple infection there is a daily paroxysm. Examination of the blood will reveal the different groups of infecting organisms.

Estivoautumnal Fevers (*Hæmaphysalis falciparum* [quotidianum]; *Hæmaphysalis falciparum* [tertianum]).—According to Marchiafava and Big-nami, confirmed by Craig, these fevers are caused by two distinct (crescent-forming) organisms, one of which completes its cycle of development in twenty-four hours (quotidian), the other in forty-eight hours (tertian). Either may give rise to fulminant symptoms, but about 75 per cent. of the cases of pernicious malaria are caused by the tertian variety. A remittent course, and various forms of irregular temperature curves are exceedingly common.

The estivoautumnal parasites may not be found, or may be found in small numbers only, in the peripheral circulation, but splenic puncture or post-mortem examination of the deeper tissues will reveal them—perhaps in considerable multitude.

We shall first consider the uncomplicated fevers, leaving the pernicious types for later discussion.

Tertian Estivoautumnal Fever; Malignant Malarial Fever (*Hæmaphysalis falciparum* [tertianum]); **Prodromal (Non-pernicious) Types**.—As in the ordinary tertian infection, the paroxysm recurs every forty-five to forty-eight hours with the sporulation of the successive broods of the parasite.

Cold Stage.—Distinct chill may not occur. In the majority of cases, chilly sensations creep along the spine, thighs, and buttocks. There is frequently an intense headache with profound weakness, muscular aching, and mental depression. The tongue is coated. The skin presents the usual goose-flesh appearance. The pulse is accelerated, feeble, and of poor volume; the respiration, rapid. The temperature may reach 103° F. or higher. The chilly stage, less intense than the ordinary tertian chill, lasts little longer than half an hour.

Hot Stage.—Sensations of warmth and flushing supervene upon the gradually fading cold stage, until the patient complains of the heat. The skin is red, dry, and hot; the eyes, injected. Severe pain may develop in the back, limbs, or abdomen. Nausea, vomiting, and diarrhea are not uncommon; the urine is increased in amount. The pulse is rapid and jerky; the respiration is accelerated. This stage may last some sixteen or twenty hours. The temperature in a typical instance at first continues, perhaps with slight fluctuations, to rise and then maintains its height; a slight remission occurs, followed by a rapid fall, not, however, to normal (pseudocrisis), and a renewed (pre-critical) rise which is, at times, preceded or accompanied by chill. This may last for some time. Then comes the true crisis, accompanied with perspiration, more or less profuse. The duration of the febrile stage may be from twenty to twenty-four or even thirty-six hours.

Sweating Stage.—With the first fall in temperature and slight sweating, the symptoms decline, and with the crisis, as a rule, they disappear. The

period of normal or subnormal temperature (intermission) may last but a few hours, when another paroxysm ensues. The temperature curve in uncomplicated cases is absolutely diagnostic: 1. Initial rise. 2. Slight remission. 3. Pseudocrisis. 4. Pre-critical rise. 5. True crisis.

In **double** infections, there may be daily paroxysms of true type; or remittance, rather than intermittence be manifested. In **multiple** infections there may be a subcontinued or highly irregular form of fever. These forms greatly resemble typhoid fever, and have been mis-called *typhomalaria*. When they take on a grave type, with stupor and delirium, jaundice, intractable vomiting, profuse diarrhea, enlarged spleen, macular eruptions, dry coated tongue, sordes, and gingival hemorrhages, the resemblance to certain cases of typhoid may be still more marked. No discrimination is more important, since to mistake typhoid fever for malaria, is equally as harmful as an error in the opposite direction.

Quotidian Estivoautumnal Fever; Malignant Malaria (*Hæmamaeba falciparum* [quotidianum]).—Occurring with the daily sporulation of the parasites, the *paroxysm* is characterized by more or less severe chill and profuse sweat, with constitutional disturbances similar to those described in the preceding section. The temperature curve, however, shows abrupt rise and abrupt fall. The attack lasts some eight or ten hours. Not rarely, the fever assumes a remittent, subcontinuous, or irregular type, as paroxysms merge into one another more or less closely. The discrimination from typhoid fever is here also difficult and important.

PERNICIOUS MALARIA.

From the suddenness and severity of their symptoms, and from their high mortality, certain forms of malaria are termed *fulminant* or, more commonly, *pernicious*. The term *malignant*, formerly used synonymously, has now been extended, improperly, to all fevers caused by crescent-forming organisms (*estivoautumnal fevers*).

VARIETIES.—Pernicious forms of malaria are classified in two ways: 1. According to the temperature curve, as *tertian*, *quotidian*, *remittent* or *larval* forms. 2. According to the character of the clinical manifestations, as of the *comatose*, *delirious*, *tetanic*, *gastric*, *dysenteric*, *choleraic*, *algid*, *pneumonic*, *hemorrhagic*, *cardialgic*, and *bilious* types.

The chief clinical forms will here briefly be considered.

SYMPTOMS AND DIAGNOSIS.—The pernicious character of the attack may be evident from the first, or may show itself only after two or three paroxysms.

Coma may appear in two ways, as follows:—

1. With *sudden* onset, so sudden in fact, that the patient—often one who has suffered from previous infections of milder type—is stricken and falls to the ground, perhaps to die before regaining consciousness. This type is not rarely mistaken for apoplexy. The face is suffused, the skin hot and dry, and the pupils contracted. Full, bounding pulse and stertorous breathing complete the resemblance. The temperature may be relatively high (103° F.), or subnormal, and death may ensue within forty-eight hours.

2. With *gradual* oncoming, after more or less severe paroxysms. Delirium, restlessness, and mental depres-

sion are more than commonly marked, and the patient slowly passes into somnolence, progressing to coma. In certain cases the icteric hue of the skin and the yellowness of the conjunctiva may give rise to a mistaken diagnosis of yellow fever. In those suffering from chronic malarial anemia a peculiar pallor may be present.

In the typical attack the skin is hot and dry and may exhibit slight punctate hemorrhages (petechiæ). The pupillary symptoms are not constant. The tongue is coated and tremulous. Respiration is slow and quiet, but may become quickened and stertorous; toward the end it may assume the Cheyne-Stokes type. Sphincter control is lost. Paralysis or hemiplegia may follow. A full bounding pulse becomes rapid, irregular, and weak. As a rule, the patient rapidly passes into general collapse, and death shortly ensues. Sometimes, however, a period may follow in which the temperature falls, profuse perspiration takes place, and to all appearances the patient is slowly gaining, when a second, or perhaps a third paroxysm supervenes, and terminates fatally. The gradual form of coma, whether continuous or intermittent, may last from two to four days. While it is attended with a high mortality, recovery, at times surprising, may take place.

The temperature curve varies. It may be high or low—even subnormal—and corresponds to no type. 112° F. and 96° F. have both been recorded. In all cases a blood examination should be made at the earliest possible moment.

In either form of comatose attack, certain muscles may be the seat of local spasm, giving rise to jerking or contractures of the limbs, trismus, deviation of the eyeballs, etc.

Among other cerebral types that may be mentioned are the *delirious* form, characterized by hallucinations or maniacal excitement; the *tetanic* or *eclamptic* form, characterized by convulsions, and common in children, in whom it may be mistaken for cerebro-spinal meningitis; the *hemiplegic* form, characterized by complete monolateral or even bilateral paralysis; the *cephalgic* form, with profound headache, which may be confounded with meningitis, typhus or typhoid fever, etc.

Algid Form.—This takes its name from the marble coldness of the body. It is one of the most fatal of the pernicious types. The characteristic symptoms may develop after one or more paroxysms of common type, during the febrile or sweating stage, or they may initiate the entire reaction.

A characteristic Hippocratic facies, with sunken eyes, dilated pupils, drawn face, and pinched nares, may be presented. The entire body is cold, pallid or cyanotic, and bathed in a profuse cold sweat. The tongue is dry and cold, and coated with a white fur. The pulse is rapid, thready, compressible, and intermittent. Respiration is shallow and irregular. The abdomen is retracted, and the enlarged spleen becomes readily palpable or even visible. The mind may be clear, but the patient is apathetic, and the heart sounds inaudible. As death approaches the pulse becomes imperceptible. Unaware of the increasing coldness of the body, the patient complains of heat. Rectal temperature is elevated. Death supervenes in a few hours, despite heroic treatment.

Syncopal Forms.—Closely allied to the algid form is the condition in which even the slightest exertion of the pa-

tient as turning in bed, or lifting the hand, brings about a syncopal attack. Symptoms of collapse dominate the picture, and even should the patient come safely through one paroxysm, a succeeding crisis, unprevented by treatment, may carry him into the great unknown.

Of kin to the algid type is likewise the *sudoriferous* form. At the end of the febrile stage, excessive and prolonged sweating occurs, accompanied with symptoms of collapse, usually fatal.

Choleric form Type.—In this type, gastroenteric symptoms, with a tendency to algid phenomena, give rise to a symptom-complex so closely resembling the algid stage of Asiatic cholera, that in climates where both exists, only a blood examination or bacteriologic study can differentiate between them. Active treatment is usually followed by recovery. The principal symptoms are vomiting, profuse diarrhea, and fever. The diarrhea leads to profound collapse, with the usual train of phenomena. The stools are liquid, flecked with blood, and like the rice-water stools of cholera. Severe abdominal pain and cramps in the extremities are common. Death ensues in inadequately treated cases.

Another form, marked by loose, blood-stained discharges from the bowel, is the *dysenteric* type, observed in tropical climates. Algidity and collapse are wanting, and when properly studied and treated, the condition usually clears up.

In the *bilious* form, a symptom-complex of jaundice, vomiting of bile and blood-stained fluid, accompanied by epistaxis, frequently hematemesis, and serous, bile-stained, or bloody alvine discharges, follows a well-defined

paroxysm. The temperature becomes more or less remittent, and continuous delirium or even coma, may develop. Severe epigastric or abdominal pain, constant hiccough, and at times tympanites, add to the distress. The urine is scanty and deeply discolored. Untreated, the patient will succumb. Active therapy usually brings about recovery.

The *cardialgic* and *gastralgic* form is distinguished by severe, often agonizing, pains in the epigastrium occurring during the chill or febrile stage of the paroxysm and mitigating toward its end. The pain may be referred to the spinal column. The attack is often accompanied by an oppressive sense of thoracic fullness, hiccough, vomiting, and hematemesis. Intestinal symptoms may be associated. Collapse may ensue, with its usual train of symptoms.

Hemorrhagic types are relatively infrequent. As the name implies, they are characterized by bleeding, which may be the only unusual phenomenon, or may complicate any of the other syndrome groups. The hemorrhages may occur anywhere, and be slight or overwhelming. Their chief incidence is perhaps from the nasal, gingival, buccal, alimentary and respiratory mucous membranes; but hematuria, and conjunctival and retinal hemorrhages are not unknown.

Pneumonic and Pleuritic Forms.—The chief symptoms are thoracic pain, dyspnea, cough, and not rarely hemoptysis or bloody sputum. Physical signs are not constant. At times percussion resonance may be unimpaired, while auscultation reveals merely showers of fine bronchial râles, extensively diffused, but without bronchial breathing. At other times there is distinct localized or disseminated dull-

ness, indicative of congestion and blocking of the lung capillaries. The characteristic phenomena may appear suddenly or develop in the course of what seems to be one of the milder forms of attack. They may clear up suddenly and as suddenly reappear. This intermittence and recurrence, often periodic, is the chief diagnostic sign by which an actual complication by lobar or lobular pneumonia may be excluded.

ETIOLOGY.—The pernicious forms of malaria depend upon the same organisms as the milder forms, but the great preponderance of fatal cases is caused by the estivoautumnal (crescent-forming) parasites, and of these the tertian parasite is the chief offender. It is generally believed that the infecting organisms develop toxins of unusual potency. Heat and exhaustion, however, are powerful contributing causes.

Bastianelli and Bignami, confirmed by Bass, attribute pernicious symptoms to a localization of the parasites in the brain or other organs. Frequently the lumina of the capillaries are occluded with infected red cells, pigmented leucocytes, free pigment masses and debris. At times, and particularly in the bowel, necrosis and ulceration ensue. The virulence and number of the infecting organisms, and the resistance and environment of the patient also affect the result.

In temperate climates the few cases that occur usually appear in summer or autumn. The morbidity increases (in number as well as duration) as the torrid regions are approached, while in the tropics and subtropical regions pernicious malaria may occur throughout the year.

Certain classes of persons seem more susceptible than others:—

1. Individuals who have suffered from repeated attacks of malarial infection and have not been properly treated, especially those who neglect quinine prophylaxis.

2. Those whose work exposes them to the torrid rays of the sun for long periods. They are especially liable to the comatose form.

3. Strangers to malarial districts.

4. Alcoholics.

5. Persons who are ill nourished, and especially sufferers from acute or recurrent disorders of the alimentary tract. These may develop choleraic and dysenteric syndromes.

LATENT AND MASKED MALARIA.—A *latent* malarial infection is one in which the parasites, though present in the system and frequently found in the blood, give rise to no distressing symptoms.

According to Plehn, urobilinuria reveals latent malaria. Schlesinger's method: To the urine add an equal quantity of saturated zinc acetate solution in absolute alcohol in a test-tube. Shake well, add a few drops of Lugol's solution, and shake again. The filtered mixture then shows fluorescence according to its urobilin content.

Latent malaria may be roused or simulated by arsphenamin preparations. In Berlin, tropical malaria had seemed endemic until traced to arsenates; 37 per cent. of the "malaria" patients had never left Germany. Rosenberg (Deut. med. Woch., June 22, 1923).

A *masked* infection is one in which the symptoms are either (1) atypical, or (2) obscured by the symptom-complex of a concurrent ailment, usually another infection. The crescent-forming parasites seem to be responsible for the majority of cases.

Malaria mimics other diseases. In a tropical town a man arrested because he is extremely noisy and apparently drunk may next morning be

found very ill or dying and the blood examination show many subtertian parasites, indicating pernicious malaria. A man brought to a hospital in a stuporous or melancholic condition, with normal or subnormal temperature, may be considered a lunatic, but a blood film leads to the true diagnosis of pernicious malaria. A man never known to have malaria, attending a concert, slipped off his chair, unconscious, and was thought apoplectic; a blood examination showed malarial parasites. Pernicious malaria may produce a clinical picture by no means unlike cerebrospinal meningitis. A boy aged 12 was brought to a hospital, unconscious, with dilated pupils, very slight corneal reflex, involuntary passage of urine, twitching of the fingers and toes, rectal temperature 103°, tongue coated, and spleen enlarged. Lumbar puncture was negative but subtertian parasites were found in the blood. In another case, a male aged 25, the malarial condition resulted in acute mania so violent that the patient had to be put in chains and under guard. Under repeated 10-grain injections of quinine bihydrochloride he recovered in 14 days. Kamar (Jour. of Trop. Med. and Hyg., Dec. 15, 1917).

Some cases may be termed both masked and latent, *i.e.*, the patient is free from symptoms for long periods, and then develops symptoms which are not, on the surface, suggestive of malarial infection.

[Thus in 1 case observed by the senior writer there had been for twenty years annual recurrences of severe gastroenteric disturbance, with nausea and vomiting, or with anorexia especially marked. Careful search, based upon the history of annual periodicity, failed to discover parasites in the peripheral blood, but upon the administration of 0.5 Gm. (8 grains) of quinine and urea hydrochloride subcutaneously they appeared, at first in small numbers, then rapidly multiplying. Continued, adequate medication was followed by recovery from the attack, but in the following autumn recurrence took

place as usual. The same experience was repeated: (1) No organisms discoverable; (2) appearance of crescent-forming parasites in blood-stream after small dose of quinine; (3) recovery upon adequate use of quinine. This time, however, the use of quinine was continued for six months, and arsenic was also given from time to time. Quinine was then resumed a month earlier than the time of annual recurrence, and continued for three months. After that no further trouble was experienced. S. SOLIS-COHEN AND L. SOLIS-COHEN.]

In some cases, a semiannual periodicity has been observed. Altogether, in thirty years, the senior writer has seen about a dozen such cases; but in highly malarious regions they must be more common, and it is strange that they have received comparatively little attention from writers and students.

In *unmixed masked malaria*, *i.e.*, infection with atypical symptoms, the morbid picture may be febrile or afebrile, with local or general disturbances. As a rule, careful observation will detect more or less regular periodicity of manifestation, or a tendency to periodic crises. Myalgias, arthralgias, cephalalgias, and neuralgias are among the most common varieties; but visceral disturbances, often painful and critical, often occur. The so-called "brow-ague" often assumes the type of *sun-pain*, *i.e.*, pain in and over the eyes, usually accompanied by tenderness on pressure at the supraorbital or infraorbital notch, or both, appearing in the morning, and disappearing at sundown. It may be unilateral or bilateral, and may appear daily or on alternate days, weekly or fortnightly, or irregularly.

There are cases of malaria in which the sole clinical manifestation is some symptom not ordinarily considered

characteristic of the disease, together with a very moderate degree of intermittent or continuous fever and the constant presence of black, blue, as well as sometimes of ochre pigment in the blood and urine. This larval type of malaria does not follow ordinary acute paroxysms, but appears *ab initio*. No plasmodia are to be seen in the blood at the time. The following symptoms were found related to the appearance of the pigments in the urine: (1) Sensation of cold in the lower limbs and back; (2) edema of the extremities or face; (3) trigeminal or intercostal neuralgia; (4) peripheral neuritis with paraplegia of the flexor variety; (5) attacks of dizziness, and (6) pain in the epigastrium. The black pigment is always to be seen microscopically in the urine, provided the slide be moved around to set the pigment particles in motion. The blue particles are equally pathognomonic, but are much fewer in number and usually smaller than the black. Ten cases illustrating the various forms of larval malaria are reported. Recovery always followed the use of a *cholagogue* or small doses of *quinine* for a few weeks. C. L. Urriola (Paris méd., Oct. 25, 1913).

Various procedures for the detection of latent malaria by driving the parasites into the peripheral blood stream have been described. Making tests with a considerable number of agents, the writer found administration of *strychnine nitrate* most effectual. In healthy subjects in malarial districts this caused the appearance of parasites in 36 to 50 per cent.; in long-standing cases free of attacks for over 6 months, in 47.5 to 62 per cent.; in cases free of attack for 4 to 6 months, in 60.2 to 65 per cent., and in those free of attacks for 2 to 3 months, 62 per cent. in adults and 73 per cent. in children. I. Di Pace (Dec. 18, 1922).

Whatever the type of infection, the organisms are found in relatively small numbers, but in all stages of development. In some cases of latent infection a complete cycle of the

malarial organism within the spleen has been demonstrated *post mortem*.

Among the **concurrent**—*i.e.*, mixed—infections that may *mask* malaria or *be masked* by malaria, the most common are tuberculosis, dysentery (amebic or bacillary), and typhoid fever.

It can readily be seen that malaria carriers (whether subjects of latent or masked infection or both) are a source of perennial danger to any community living in a region infested by *Anopheles* mosquitoes. Henson has entered a justifiable plea that more attention be paid to prophylaxis from the viewpoint of man as an infective focus.

COMPLICATIONS AND SEQUELÆ.—Complications.—The complications of malaria are for the most part accidental; *i.e.*, they arise from pre-existing disease or mixed infection, and are not a necessary result of malarial intoxication. Sometimes, however, they may be the result of purely mechanical causes, as when circulation is obstructed by infected cells, *débris*, etc.

Acting upon the nervous system, malarial toxemia may give rise to cephalalgia, neuralgia, neuritis,—often multiple,—or acute mania. Paraplegia, hemiplegia, and other paralysees are more frequently of mechanical origin.

When malaria attacks the brain, it may simulate any form of cerebral disease, but in a general way three types may be recognized. These are: (1) The comatose. (2) The motor irritative type, also with coma, but with motor symptoms ranging from muscular twitchings to clonic convulsions. It may simulate uremia, hysteria, or tetanus. (3) The motor depressive type, which is rare. It may cause monoplegic, hemiplegic or para-

plegic paralysis, usually subsiding with the paroxysms. In the majority of cases any mental disturbance quickly disappears. In all cases the estivo-autumnal organism is the cause. J. F. Patterson (Jour. Amer. Med. Assoc., Nov. 15, 1913).

Case of tropical comatose malaria in which, after slight febrile attacks for some weeks, evidences of meningitis set in abruptly. The first spinal puncture was negative for parasites, though bloody. Three days later it contained parasites of tropical malaria. Death followed in spite of quinine. Higier (Münch. med. Woch., Apr. 3, 1925).

Acute bronchitis is the most common respiratory complication of malarial infection. Lobar pneumonia, however, is not uncommon, and is a secondary infection, not due to the malarial parasite, as formerly supposed. Malaria may diminish the resistance to pneumococcic or other infection, but there is no other relationship between the original and the complicating malady. Pneumonia may mask the malarial symptoms, or the reverse may be the case. Ordinarily, however, the course and symptoms resemble those of uncomplicated lobar pneumonia with perhaps an impression of recurrent tendency to chill and fluctuation of temperature. The prognosis is necessarily grave. Bronchopneumonia occurs less frequently than the lobar form and may be produced by the plasmodia. Chronic fibroid pneumonia may supervene. Pleurisy has been observed as a concurrent infection.

Out of a total of 115 cases of malaria treated by the writer during an epidemic of influenza, 112 suffered from the latter disease. Of the 50 in which pulmonary complications occurred, 42 or 36.52 per cent. died, even though quinine had been exhibited in large doses. Colalè (Políclinico, Jan. 26, 1919).

Tuberculosis and malaria may co-exist. Marchiafava states that when tuberculous patients contract malaria, miliary infection is likely to be the result. These observations have been confirmed by Craig.

Organic disease of the heart may complicate malaria, and functional disorders are not uncommon. Bradycardia and tachycardia have been observed.

Albuminuria accompanies rather than complicates malarial infections. Thayer reports 46 per cent. of instances and Craig 50 per cent. Acute, subacute, or chronic nephritis may complicate as well as supervene upon a malarial infection. Orchitis and epididymitis may occur. Mannaberg also reports gangrene of the penis and of the labia.

Cases associated with jaundice of hemolytic type, enlarged liver, enterocolitis, Addison's disease, Raynaud's disease and Parkinson's disease described. Comessatti (Morgagni, Jan. 31, 1922).

Edema may be the initial sign of the disease. The kidneys are not responsible for it, and it yields readily to quinine, which should be given in increased amount, mainly by the intravenous route. Sainton, Richet, Jr., and Schulmann (Ann. de méd., Feb., 1922).

A mulatto laborer suffered intensely from throbbing pains in the hands and feet, complained of abdominal cramps and prostration, and had symmetrical gangrene. Under quinine and local treatment he recovered, after separation of the sloughs. J. B. Guthrie (New Orleans Med. and Surg. Jour., Mar., 1922).

The most common of gastroenteric complications is dysentery in both its bacillary and amebic forms. This co-existence is common in the tropics. The dysenteric symptoms are always aggravated by the malaria, which

may remain latent. Quinine ameliorates both processes.

Typhoid fever and malaria frequently coexist. Deadrick records from the literature 215 cases in which the presence of parasites and bacilli, together with a positive Widal reaction, were demonstrated. The organisms were chiefly of the ordinary tertian type, but crescent-forming parasites were found also, and the senior writer has seen a number of such cases. Craig has reported the only case of quartan infection complicated with typhoid of which the writers have knowledge. The old idea that a hybrid disease (so-called typhomalaria) is produced, is incorrect. The condition is one of concurrent infection. The malaria may occur primarily, may appear during convalescence, having been latent, or may even be acquired during the course of typhoid fever. In all cases the prognosis is rendered more grave by the double infection.

The effect of malaria upon pregnancy is important. In malarial districts, a latent infection is likely to flare up during gestation and to produce premature labor. This may be one of nature's protective processes. Henson has observed abortion in one-fourth of the cases of estivoautumnal infections complicating pregnancy. During the puerperium malaria may cause considerable difficulty in diagnosis, unless the blood is examined in order to differentiate it from septic infection.

Infants less than a year old seem to display resistance to malaria, both against acquiring it and against its effects. Malarial cachexia was observed to occur most frequently between the ages of 3 and 7; if children thus affected survive, they acquire

lasting immunity. The spleen is not always enlarged even in these severe cases, and the anemia is not always intense. Various types of the hematozoa were found combined in the blood in some cases. Gastrointestinal disturbances were the main complication of malaria in children, but the blood findings were negative in 92 cases of febrile diarrhea ascribed at first to malaria. Malarial nephritis has scarcely ever been observed in a child, but epistaxis, purpura, vomiting of blood, cirrhosis, urticaria, and ascites are frequent complications, as also convulsions and delirium. J. P. Cardamatis (*Grèce médicale*, May 15, 1909).

Among 30,000 cases of malaria admitted to the Colon Hospital during eight years, only 3 instances of spontaneous rupture of the spleen were noted. Conclusions: Spontaneous rupture of the malarial spleen occurs in rare instances; the organ does not necessarily have to undergo a great degree of enlargement for spontaneous rupture to occur; very deep palpation or forcible percussion of the enlarged malarial spleen should be avoided; exploratory puncture of the spleen for diagnostic reasons is not without danger; the treatment of spontaneous rupture is early **tamponade** or **splenectomy**. Noland and Watson (*Annals of Surg.*, Jan., 1913).

Sequelæ.—The sequelæ of malaria may be manifested in any or in all of the organs and tissues of the body. Only those affections, however, can rightly be classed as sequelæ which are owing to the toxins generated during the active stage of the disease, to the hemolysis, or to the mechanical interference with circulation by the blocking of the capillaries, and which manifest themselves after the subsidence of the exciting infection. This point cannot always be clearly established, and in some cases de-

scribed as of postmalarial disorder, the plasmodia can still be demonstrated. Recovery, indeed, may depend on their discovery and their consequent treatment by quinine. We shall not here attempt to discriminate between true sequelæ and symptoms developing under continuous infection after the disappearance of paroxysms.

Nervous sequelæ are most numerous after estivoautumnal infections, but may follow the course of other infections. J. M. DaCosta, of Philadelphia, was the first to report a case of hemiplegia. Mannaberg describes cases of aphasia, monoplegia, and paraplegia. Conditions closely simulating multiple sclerosis have been observed by Torti, Bignami and other observers. Multiple neuritis and peripheral nerve disorders, neuralgias, and neurasthenic conditions are likewise reported.

Among *mental disorders*, melancholia, mania, and delusional insanity sometimes occur as postmalarial phenomena. Craig found a mild melancholia to be the most common mental affection following malarial fever.

When the blood-findings are positive, the nervous and mental phenomena show rapid and marked improvement under quinine, complete recovery being the rule.

Upon the heart and blood-vessels, according to common and authoritative opinion, malarial toxins rarely have sufficient effect to cause sequelæ of serious import. The senior writer, however, has observed cardiac myopathies that he could attribute to no other cause.

A true acute or chronic ulcerative enteritis and, although rarely, gas-

tric ulcer, may result from a localization of the parasites in the mucosa of the gastroenteric tract.

Kelch and Kiener describe both acute and chronic glomerular nephritis, and likewise, acute and chronic granular nephritis. The glomerular types give rise to chronic parenchymatous nephritis, and the granular type to subacute and chronic interstitial nephritis. In 112 cases of acute nephritis of all types, Thayer observed 21 (or 18.7 per cent.) of malarial origin. In 1832 malarial sufferers, the same observer noted 4 cases of chronic nephritis.

Albuminuria, with few or no casts, is also of common occurrence. Amyloid degeneration, polyuria, and glycosuria have been reported in rare instances.

Estivoautumnal infections give rise to the majority of the kidney lesions. Craig observed that 3 per cent. of all estivoautumnal fevers are followed by nephritis, but that the latter is very rare (0.5 per cent.) after quartan and ordinary tertian cases.

Hypertrophic malarial hepatitis has been reported as following repeated estivoautumnal infections. It seldom gives rise to clinical trouble. The senior writer and others have recorded cases of biliary cirrhosis, pursuing the usual course, with splenic enlargement. It is a disputed point whether a true atrophic cirrhosis of the liver exists as a malarial sequel, as the affection is found in about the same proportion of persons in malarial districts as elsewhere.

Floating or wandering spleen and abscess of the spleen occur infrequently. The enlarged spleen or ague-cake, often associated with enlarged liver, is common. Cases of splenome-

galic anemia with hemorrhage and leucopenia, in all respects resembling Banti's disease, have been observed in persons who had recovered from malaria, but Osler excluded them from the category of malarial sequelæ.

In one such instance in the senior writer's service, his quinine method caused the appearance in the peripheral blood of organisms recognized by R. C. Rosenberger as atypical malarial hemamebæ.

Orchitis and epididymitis have been reported by Zienian. These are of rare occurrence.

Among the eye affections that follow malaria are amaurosis and retinochoroiditis; but these are sometimes attributed to the quinine. Keratitis and suppurative choroiditis have likewise been observed.

Intermittent otalgia, intermittent deafness, labyrinthine vertigo, and suppurative otitis media are among the ear affections observed.

Post-malarial anemia may be very grave, sometimes closely resembling pernicious anemia. It may be uncomplicated or form part of the complexus known as *malarial cachexia* (*q.v.*). Severe secondary anemias frequently follow both ordinary and estivoautumnal infections, but as a rule, yield readily to arsenic and iron.

PATHOLOGY.—Acute Malaria.—

As the benign malarial infections seldom lead to autopsy, our knowledge of the pathological changes induced by malarial fevers is based chiefly upon observation of the pernicious and estivoautumnal types.

The writers hold that the adrenals are responsible for the attacks of coma, the algid and other choleriform symptoms of pernicious malaria, these organs showing acute hemor-

rhage and degeneration. Paiseau and Lemaire (*Presse méd.*, Dec. 4, 1916).

In the Salonica Army, sudden death or early death was common, 57 per cent. dying within the first 48 hours after admission. The adrenals showed most marked changes. Dudgeon and Clarke (*Lancet*, Aug. 4, 1917).

The writer observed 3 cases of malaria indicating acute insufficiency of the adrenals, and urges the use of **adrenalin**. Fraga (*Revista Ibero-Am. de Sc.*, July, 1918).

Of these changes, *melanemia*, or the widespread intravascular deposition of a pigment termed melanin, is the most striking. Melanin is a product of hemoglobin elaborated by intracorpuseular parasites in the course of their destructive activity.

Melanin must not be confused with hemosiderin, an ochre-colored pigment found in the tissues, and which is derived from the hemoglobin of corpuscles not attacked by the parasite. It occurs in the form of dark brown or black granules, which tend to clump when situated in the viscera. When liberated by the completed segmentation of the sporulating parasites, it is largely taken up by the leucocytes and by them deposited principally in the capillaries of the brain, liver, spleen, and bone-marrow.

Occasionally melanin is found free in the blood or in the tissues, which latter it can reach only by diapedesis of the leucocytes or rupture of the capillaries. Hemosiderin, on the other hand, is found only within the tissues. It is deposited in the liver, kidneys, spleen, and bone-marrow in the form of yellow granules, clumps, or small ochre-colored masses. In contrast with melanin, it is found within the endothelial cells and Kupfer's liver cells.

[Melanin is insoluble in strong acids, but soluble in ammonium sulphide, and is decolorized by potassium and ammonium salts. No trace of iron has yet been demonstrated in it.]

[Hemosiderin gives an iron reaction to the ferrocyanide test, and turns black when treated with ammonium sulphide. It is insoluble in strong acids and alkalis, alcohol, and water.]

The degree and extent of the melanosis largely depend on: (1) the type of the parasitic infection; (2) its virulence, and (3) the distribution of the parasites. Thus in quartan infection, the parasites are found chiefly in the peripheral blood-stream. The internal organs are the chief habitats of the parasites in the estivo-autumnal types, while in the simple tertian fevers the plasmodia are found in large numbers in both the internal organs and the peripheral blood. Numerous parasites, giving rise to an overwhelming infection, will tend to a greater red-cell destruction and elaboration of abundant pigment.

The diagnostic importance of loose blood pigment in the blood in malaria was pointed out by Risquez (*Risquez's sign*). A little sulphuric acid, taken up by capillary attraction between the slide and cover-glass, enhances visibility of the melanin by destroying the blood cells and hemoglobin while leaving the pigment unchanged. This sign is positive even after disappearance of the parasites from the blood under quinine treatment. Villegas Ruiz (Gac. méd. de Caracas, Oct. 31, 1925).

The distribution of malarial pigment throughout the organs gives rise to the characteristic striking slate-gray color noticed by such early observers as Laveran, Stoll, and Bright.

The *spleen* is enlarged, sometimes enormously so, especially in pro-

longed and repeated infections. It is discolored, the hue varying from a light chocolate to jet black. The capsule is tense, smooth, and may even rupture. The cut surface drips blood; the pulp is soft; the Malpighian bodies may stand out prominently. In very recent infections and in the estivoautumnal types, the splenic enlargement is often slight. Microscopically, the sinuses are congested and dilated, containing numbers of plasmodia in all stages of development, including crescents. Numerous large mononuclear and polynuclear cells (macrophages), laden with pigment, are also found. The small lymphocytes, Malpighian bodies, and endothelial cells may contain slight amounts of pigment. Free pigment is found throughout the parenchyma.

Areas of focal necrosis are sometimes observed. The connective tissue is likely to be increased in repeated and chronic infections. Thrombosis in the splenic sinuses from congestion and massing of pigment are not uncommon.

The *kidneys* rarely show evident pigmentation, except in cases of black-water fever, in which both pigmentation and hemorrhage are marked. Ordinarily, there is slight enlargement and the smooth capsule is easily stripped. Sometimes the kidney resembles that of acute nephritis, with small punctate, cortical hemorrhages. Congestion may be present, with cortical enlargement. Microscopically, the epithelium shows a slight pigment content. Casts and amorphous masses may be found in the tubules. The glomeruli and intertubular capillaries may contain melanin, a few parasites, leucocytes,

and macrophages. Signs of an acute nephritis may also be present.

The *liver* is commonly enlarged and congested. The hyperemia is responsible for much of the increase in weight. Pigmentation gives to the organ a brown or blackish color. The gall-bladder is distended with dark bile. The cut section exhibits a markedly congested surface of a slate-gray color.

Microscopically, the capillaries of the portal and hepatic veins are found to contain parasites, and parasites and splenic macrophages are found in the portal veins as well. The endothelial cells and Kupfer's cells contain pigment. Barker has observed areas of focal necrosis from capillary thrombosis. The cells of the parenchyma become swollen, vacuolated, atrophied, and necrotic.

The levulose tolerance test showed slight disturbance of the glycogenetic function in some ordinary cases of acute malaria. Ingestion of dextrose or levulose is indicated, especially in severe cases, to protect the liver cells. Sinton and Hughes (*Indian Jour. of Med. Res.*, Oct., 1925).

Bone-marrow changes depend on the severity and duration of the infection. The yellow color of normal marrow is preserved in recent infections, but changes to red or black in prolonged cases which tend toward chronicity. Microscopically, parasites including sporulating bodies, and crescents, a few pigmented macrophages, and erythrocytes, are found in and around the capillaries.

The *brain* shows few changes, except in infections of long standing, or those characterized by meningeal symptoms. There may be marked discoloration of the cortex, with congestion and punctiform hemorrhagic

areas. In comatose cases, parasites in all stages of development, together with macrophages and erythrocytes, are found in the capillaries.

In the *gastroenteric* tract, the most marked changes are manifested in choleraic and allied types of infection. As shown by Bignami, the attacking parasites may be localized in the intestine. The capillaries become infected and contain free or inclosed parasites, phagocytes, and pigmented macrophages. Thrombosis and even ulceration may result. Ordinary cases will show only pigmentary changes.

In the *lungs*, non-pigmented areas of bronchopneumonia and infarction may be found. The alveolar capillaries may be blocked with parasites and macrophages, while the endothelial cells contain pigment.

The *heart* ordinarily exhibits but slight changes. The muscle may be pale, flabby, or even show fatty degeneration. The capillaries of the muscular wall may contain parasites and macrophages.

The changes in the blood as observed both during life and after death may briefly be summarized as follows: (1) A marked reduction in the number of red corpuscles, brought about (a) directly by parasitic invasion (b) as the result of poisons elaborated by the parasites during their development (c) through changes in the blood-forming glands; (2) a corresponding reduction in the number of white cells, with, in most cases, a relative increase in the large mononuclear leucocytes; (3) a marked reduction in the hemoglobin; and (4) the presence in the plasma of black and brownish-yellow pigment, in greater or less amount:

After acute initial attacks of malarial fever there occurs a rapid loss of hemoglobin and red blood cells. The hemoglobin loss, in two or three months of irregular fever, may take place to an amount of from 40 to 50 per cent. of the normal, and the reds diminish to the extent of from 2 to 2½ millions to the cubic millimeter. After the attack is cut short by treatment the recovery in these blood elements is likewise rapid. J. P. Bates (Jour. of Trop. Med. and Hyg., July 1, 1913).

Chronic Malaria.—The most important structural changes are found in the liver, spleen, and bone-marrow.

The *spleen* is usually considerably enlarged, its capsule being irregularly thickened and in places calcified. The organ is more or less hardened. Its color may be red, grayish brown, or slaty. The cut surfaces show grayish trabeculæ formed of the thickened connective-tissue stroma and vascular sheaths. The remarkable dilatation of the veins may simulate angiomata. The Malpighian bodies are ordinarily not prominent. The microscopic findings differ as the change progresses from the small, soft spleen to the "ague-cake." With the marked diminution in hyperemia which follows subsidence of the acute process, there develop miliary necrotic areas and extensive hyperplasia, involving the pulp and often the follicles. The pigment is less widely distributed and tends to become concentrated about the vessels and in the fibrous septa. Later, the macrophages which were its carriers disappear, and the pigment is found only extracellularly, in the perivascular lymph-spaces; and gradually it is completely reabsorbed.

The necrotic areas slowly undergo reabsorption; but the connective tissue hyperplasia, the vascular

dilatation, and the atrophy of the parenchyma increase. The follicles eventually become unrecognizable through fibroid degeneration. The ague-cake consists chiefly of thickened stroma and dilated vessels with but a minimum of pulp cells and follicles, and with corresponding loss of physiological function (Bignami).

The *liver* is enlarged and of increased density. The surface is smooth, the capsule thickened. The cut surfaces are irregularly pigmented in recent infection, becoming arranged as a perilobular network in long-standing cases.

Microscopically, in early cases, the capillaries are free from parasites, the endovascular macrophages have likewise disappeared, and the pigment is found only in the endothelia and in Kupfer's cells. The necrotic portions of the lobules atrophy, and the vessels dilate in consequence. Later, the pigment disappears from the lobules, being carried to the periphery by mononuclear and polymorphonuclear leucocytes which deposit it in the perivascular lymph-spaces. At the same time regenerative changes are occurring in the liver cells and the perilobular connective tissue becomes hyperplastic. In long-standing cases, therefore, there is a large hard liver of reddish color, which, on section, shows conspicuously the granular-looking lobules, surrounded by their connective-tissue stroma. The vessels are dilated; the amount of blood in the organ is increased, and the pigment is no longer visible (Bignami).

The *bone-marrow* at both the upper and the lower extremities of the long bones is red and of increased consistence. Microscopically (Bignami),

the fat has disappeared and is replaced by proliferated marrow-cells and new blood-vessels. The large and small mononuclear myelocytes are increased, and many show signs of degeneration. In addition there are numerous nucleated red blood-corpuscles of normal size (normoblasts), and a few giantoblasts or megaloblasts. The endothelium of the vessel is swollen, and the vessel walls and the stroma are thickened. The pigment disappears from the bone-marrow much sooner than from the other organs.

DIAGNOSIS.—Although clinical phenomena are important, and should be observed carefully, the diagnosis of malarial fevers today depends chiefly upon the blood-findings. The so-called "therapeutic test" as ordinarily applied for purposes of diagnosis is rapidly passing into deserved disrepute. The observation that fevers yielding to quinine are not all malarial infections has been abundantly confirmed by clinicians of the largest experience. On the other hand, such fevers do not show the prolonged "freedom-period" characteristic of uncomplicated malaria when quinine is properly employed. Hence a certain amount of dependence may be placed upon an expedient used by the senior writer for some twenty-five years. Intramuscular injection of 1 Gm. (15 grains) of quinine and urea hydrochloride will in most cases of malarial fever be followed by freedom from paroxysms, and by reduction of temperature to or below the normal line with but slight fluctuations, for a period of about six and one-half or thirteen days. Rarely have more than 2 injections on successive days been

necessary. Failure to manifest this period after 3 or 4 such injections indicates the presence of some other infection. Ianni has had similar results from the use of strychnine. A single dose of $\frac{1}{20}$ grain has been followed, in an hour or so, by the appearance of parasites in the peripheral blood. Blood tests should be made carefully and often. Both fresh and stained specimens are to be examined.

The blood is preferably taken either during a chill or a short time before it. In using an *unstained* specimen, a drop of blood is placed on a well-cleaned cover-glass and the latter gently dropped on a clean slide. Under the oil immersion objective a few of the red cells will show small hyaline bodies, moving in ameboid fashion and containing minute pigment masses in active Brownian motion. *Stained* preparations are made by spreading a thin film of blood on a cover glass, fixing by rapid passage through a Bunsen flame, and staining with Wright's stain. The sexual forms are seen only in unstained preparations, after watching for some minutes.

The following *thick film method*, without fixation, has been found more reliable than the ordinary thin smear procedure: (1) Place 3 or 4 drops of blood on a slide, defibrinating it and spreading it with a needle to obtain a disc of 1 cm. diameter; (2) dry horizontally for at least 2 hours; (3) cover with diluted Giemsa's stain (1 drop to each c.c. of distilled water) until the hemoglobin rises from the slide like a cloud (2 or 3 minutes); (4) wash laterally, keeping horizontal position, and cover for 6 to 8 minutes with diluted Leishman's stain (1 drop to 1 c.c. of water); (5) wash laterally with a gentle spray of distilled water, dry in the air in the vertical position and examine under oil immersion. The parasites appear clearly with protoplasm stained blue and chromatin ruby red.

When the examination reveals the hemameba and its type, the diagnosis of malaria is certain, but mixed infection is not necessarily excluded. Pigmented mononuclear or polynuclear leucocytes are likewise positive evidence of a malarial infection, past or present. The value of a differential blood-count showing a mononuclear hyperleucocytosis is disputed, but it may be accepted as confirmatory, though not conclusive, evidence.

When parasites are absent from the peripheral blood, they may be found in blood withdrawn from the spleen; but splenic puncture is not to be lightly undertaken, and should, in any event, be entrusted, if possible, to an experienced observer. It is better, first, to try the senior writer's method of driving the parasites out of covert by the injection of a subtherapeutic dose (0.3 to 0.5 Gm.—5 to 8 grains) of quinine and urea hydrochloride.

This method, while sometimes of service in acute fevers, is chiefly applicable in the chronic type of latent and masked cases, and frequently the organisms found upon the slide, while recognizable as forms of the hemameba, are atypical in various respects. The reaction, however, has occurred so frequently that one is inclined to look upon the absence of organisms after half a dozen injections in increasing doses from three to six days apart as virtually excluding malarial infection. Apparently in these cases the parasites are resting in a larval form, lurking in the spleen or bone-marrow, and by reproductive reaction to the paratoxic effect of quinine, they make their appearance in the peripheral

circulation. The more recent observations of Celli and of Craig go far to confirm this long-announced opinion.

An impoverished condition of the blood—i.e., low erythrocytosis with low hemoglobin content—must be taken in conjunction with the other facts obtained, and too much stress should not be laid upon anemia alone.

Clinically, the regularly recurring paroxysms and the orderly sequence of the various stages shown in an *ordinary* single or double *tertian* or *quartan* infection, together with the physical findings, are commonly sufficient to justify the diagnosis of malaria.

The irregularities frequently manifested by the *cstivoautumnal* infections, however, forbid other than tentative diagnosis without the blood-findings. A careful anamnesis should be elicited, and the prevalence of the infection and its type, in the neighborhood in which the patient resides, or has lately been sojourning, is to be taken into account.

Multiple infections with the same variety of parasite and *mixed infections* (whether of different varieties of malarial organisms or of malaria and another malady—c.g., typhoid fever) give such a varying clinical picture that an examination of the blood—or, on the other hand, bacteriologic or serologic study—is the only means of revealing the true type of infection.

When quinine has been taken before the patient comes under observation, the clinical manifestations may be so altered, both as to the periodicity and general type of the paroxysm, that one must again resort to the findings of the laboratory.

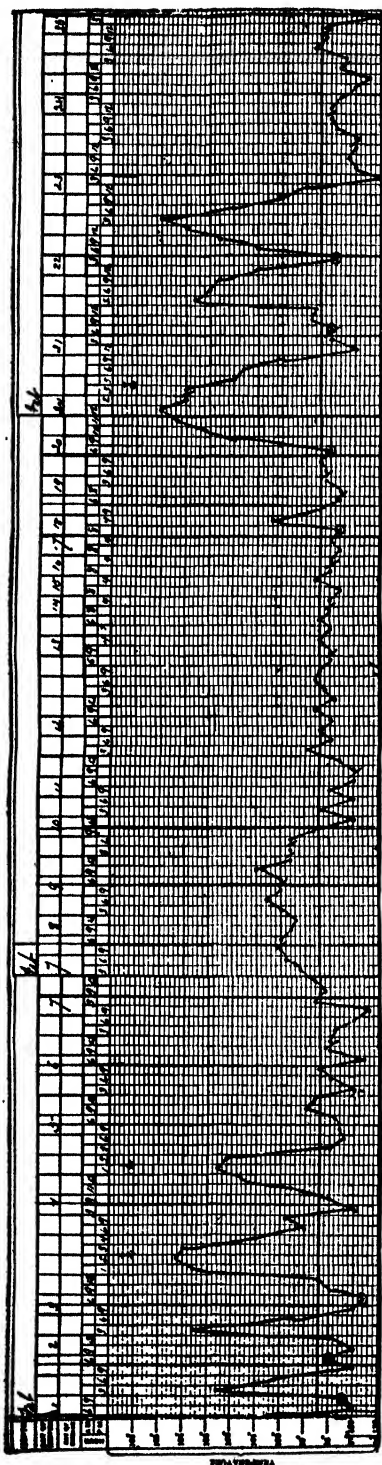


CHART I.—Temperature chart demonstrating double tertian malarial infection with freedom period of 329 hours after injection of quinine and urea hydrochloride. \circ Chill begins. t Injection given.

Differential Diagnosis.—Apart from the difficulties mentioned in the description of the pernicious forms of malaria, and in that of chronic, latent, and masked cases, there are three conditions concerning which the clinician must be constantly on guard—namely, the hectic fever of suppurations, malignant endocarditis, tuberculosis, septicemia, etc.; syphilitic fever, and typhoid fever. Every consultant has met with cases of all of these, erroneously called malaria. Sometimes there is mixed infection, which makes the diagnosis still more difficult.

Close resemblance between malaria and trench fever emphasized. But rigor is usual in malaria, provided the patient is not taking quinine. It occurs, but is unusual, in trench fever. Quinine controls the temperature in malaria in most cases, *i.e.*, it prevents more than one or two further rises to 103° or 104° F. This, of course, applies to temperate climate malaria. Quinine has no effect in trench fever. Ward (Lancet, Apr. 12, 1919).

In typhoid fever, according to the observations of J. M. DaCosta and the senior writer, made very many years ago and since then abundantly confirmed, it is common for a concurrent malarial infection to become abeyant, reappearing during the lysis or even after apparent recovery. Frequently, however, there will be a greater loss of hemoglobin than typhoid fever alone can account for, and leukemia, on the other hand, will be less marked. Malarial organisms will, as a rule, be absent from the peripheral blood during the height of the typhoid, but can in most cases be found toward its decline. The temperature curve may assume more of an intermittent or subcontinuous type than is common in typhoid, or

the thwarted periodicity may be most evident in the first week, or even in the third and fourth weeks. It is especially in cases of this kind (as also in instances of syphilitic fever of periodic, intermittent type) that the senior writer has found his quinine test valuable. If after a single injection of 1 Gm. (15 grains) of quinine and urea hydrochloride, there ensues a freedom period of not less than six and one-half days, the case is almost certainly one of uncomplicated malaria, and with return of fever, organisms will be found in the blood. On the other hand, if 3 or 4 injections on successive days (or with intervals not longer than forty-eight hours) do not cause prolonged disappearance of fever, active (but not latent, masked) malaria may be excluded, and the type of infection remains to be determined by the usual clinical and laboratory methods.

The misleading term *typho-malaria* and the cases of concurrent infection have already been dwelt upon. It is the irregular cases of estivoautumnal infection that give rise to the most confusion. A positive Widal reaction, a positive blood-culture, or a feces-culture yielding the *Bacillus typhosus* is, of course, demonstrative. In addition, the presence of motile bacilli in freshly voided urine, and a marked leucopenia without mononucleosis, are significant of typhoid infection. A negative Widal and

blood-culture, absence of motile bacilli from the freshly voided urine, mononucleosis, absence of rose spots

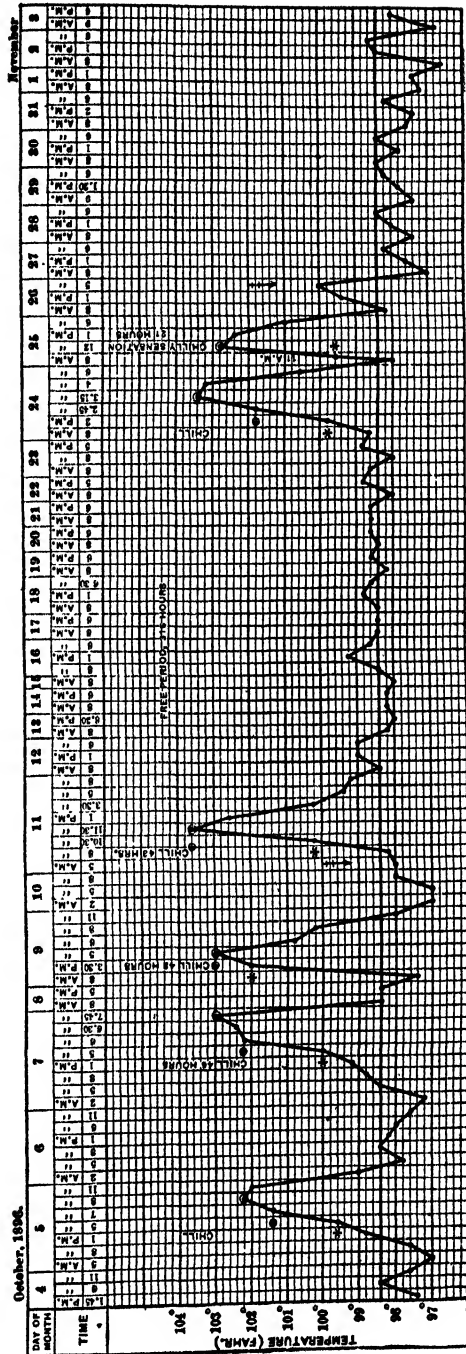


CHART II.—Tertian intermittent. Free period 316 hours. (A. B. C.; Autumn, 1896.) * Beginning of chill. † End of chill. ‡ Injection of 1 Gm. of quinine chlorhydro sulphate.

after the ninth day, and especially the finding of free pigment in the blood, even without the finding of the parasites, points rather to malaria.

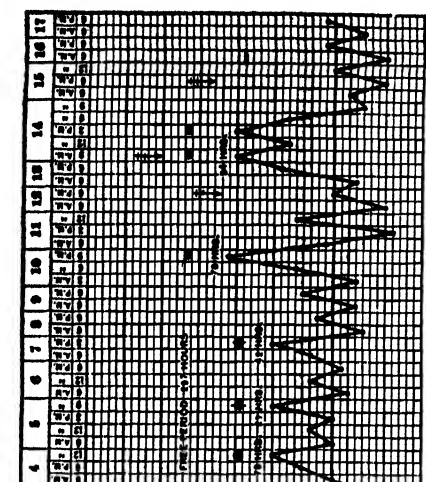
the only means of differentiation, nor is mixed infection impossible.

Dengue.—The cutaneous eruption and the severity of the muscular and bone pains, together with the blood-findings, are the principal points of discrimination.

Septic Fevers.—In all maladies accompanied by chills and fever, such as Charcot's fever, septicemia, pyemia, pyelitis, puerperal infections, malignant or infective endocarditis, or luetic infections, the history, the clinical aspect of the case, together with the symptoms and physical signs referable to each particular infection, and the all important blood-examination and cultures, will reveal the true nature of the existing illness.

Hepatic Abscess.—Although the liver is enlarged and tender, the spleen is most frequently non-palpable. Ordinarily, there is a history of dysentery, appendicitis, or gallstones, as well as a freedom from malarial hemamebæ.

Insolation.—Especially in the tropics, care must be taken not to confuse malaria and sunstroke; and even in temperate climates the mistake is possible. The junior writer recalls a case studied by him while on ward duty in the Jefferson hospital. On a hot July day, in which cases of sunstroke had been brought in by ambulances and patrols in rapid succession, a man was admitted who had been taken from an electric tram car, in a severe chill. Temperature in the mouth was 104° F., but the body, bathed in a profuse sweat, was cold. Careful questioning elicited the history of a mild attack of malaria in New Jersey, the year previous; physical examination discovered a slightly enlarged spleen, and exam-



termittent fever. Free period 297 hours. (Cosmo di G.; Summer, 1907.)
 of chill. ♦ T, rise without chills. ● Double crest temperature rise. f in-
 and urea hydrochloride.

CHART III.—Quartan
 of chill. ♦ E
 section of 1 Gm. of quinine



Other conditions may be considered briefly as follows:—

Yellow Fever.—Where the bilious, remittent, and hemorrhagic forms of pernicious malaria exist endemically in the same locality, a blood-examination revealing the plasmodia is often

ination of the blood demonstrated the tertian parasite.

Tuberculosis.—Tuberculosis may often be confounded with chronic malaria, or with a double quartan or tertian infection; and this is even more likely when the tuberculous process is aggravated by a coexisting streptococcic infection. The clinical or X-ray findings in the chest or abdomen, the absence of splenic tumor, the presence of tubercle bacilli in the sputum, feces, or urine, the absence of malarial parasites, and perhaps the cutaneous or constitutional reactions to tuberculin are the chief diagnostic facts.

Cholera and Dysentery.—Not only are there choleric form and dysenteric types of pernicious malaria, but the coexistence of the two infections—especially in the case of dysentery—is possible. Examination of the stools, and the finding of the ameba or bacillus, while examination of the blood for malarial organisms is negative, would be diagnostic.

A constant and characteristic sign of malaria is a tender point in the 9th left intercostal space, between the median and posterior axillary lines. Occasionally the tenderness is more pronounced in the 8th or 10th interspaces. Pagniello (*Semana med.*, June 17, 1920).

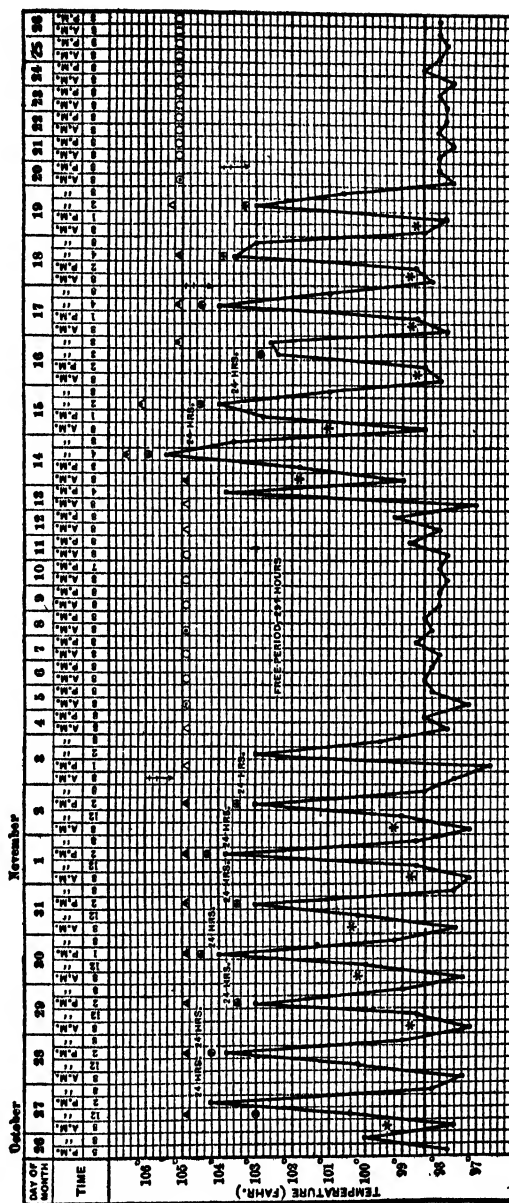


CHART IV.—Double tertian intermittent. Free period 291 hours. (Jos. D.; Autumn, 1892.) * Beginning of chill. ⊕ End of chill. † Infection of quinine and urea hydrochloride. Δ Organisms, pigmented, numerous. ◊ Organisms, pigmented, few. ○ No organisms. ⊙ Organisms, hyaline, few.

Knowledge of the commonest sites of pain in malaria proves of diagnostic value. The pain is most frequent in the back, especially in the sacral and lumbar regions, and in the head. Less common, in order, are pains below the knee, in the upper arm, lower part of the tibia and foot, forearm and wrist, and sternum. The writer looks upon

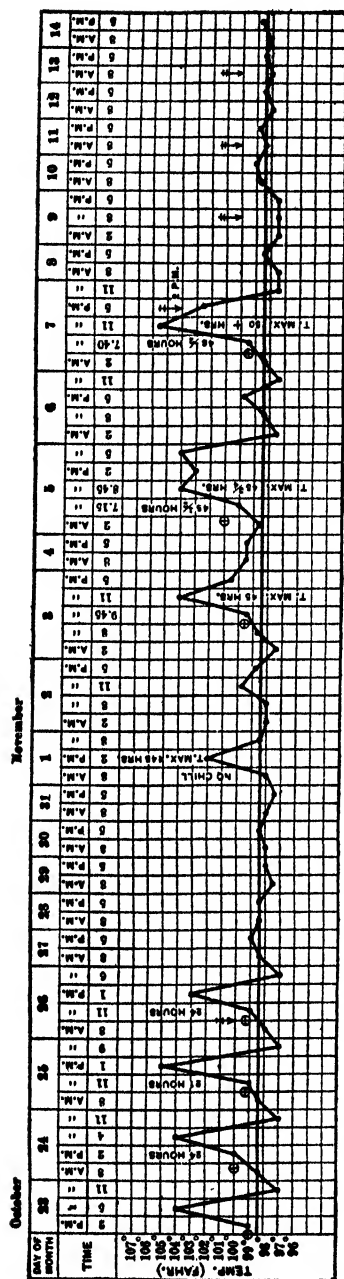


CHART V.—Double tertian intermittent fever. Free period 147 hours. Change of type to tertian. (Henry J.; Autumn, 1907.)
 ⊕ Beginning of chill. † Injection of 1 Gm. of quinine and urea hydrochloride.

these as "marrow pains," since they are uninfluenced by pressure or movement. It is known that melanin granules collect in the bone marrow, liver, and spleen. J. Tait (Canad. Med. Assoc. Jour., Mar., 1922).

Case of syphilis simulating malaria. The syphilitic manifestations, coming on 40 days after the chancre, were limited to the fever, an intense monocytosis with relative lymphocytopenia, and a tendency to hystero-epileptiform disturbances. The fever appeared every evening, preceded by a chill and followed by a sweat. After 4 months, the fever was arrested by a single injection of neoarsphenamin. Antonelli (Policlin., Aug. 31, 1925).

PROGNOSIS.—This depends, of course, on the variety and virulence of the infection, the resistance of the patient, and the treatment instituted.

It is said, on good authority, that the ordinary *tertian* and *quartan* infections tend toward spontaneous recovery.

[The writer doubts whether this is common in tertian fevers in northern countries. Many years ago he shared a hospital service with a physician entertaining that view, and succeeded to a ward in which patients had shivered and burned and sweated for several weeks,—in one case for two months,—to recover promptly under the use of quinine. This, of course, is a limited experience, but it indicates at least the probability that so-called spontaneous recovery is merely a suppression of paroxysms, the infection continuing in chronic or latent form. S. SOLIS-COHEN.]

Maltreatment, moreover, may result in a severe anemia,—a veritable dyscrasia,—draining the patient's vitality.

In the *estivoautumnal* infections, if properly treated, the prognosis is good. When continuous cinchonization is neglected, repeated relapses may occur, and the disease becomes chronic, in which case the prognosis becomes highly unfavorable, if not grave.

The outlook in *pernicious* cases of all varieties is usually very grave, especially if more than one paroxysm occur. Heroic treatment does much to better the prognosis.

When malaria is *complicated* by other infections, the prognosis is not so good as in uncomplicated cases.

Repeated *relapses*, especially of estivoautumnal infections, and when prophylactic treatment is not followed, are highly dangerous.

Relapses are most troublesome and persistent among children, always active and impatient of control, and among adults whose duties force them out again too quickly after the subsidence of the fever. In these, relapses occur at short intervals, such as two or three weeks, up to from one to three months. The intervals bear some relation to the thoroughness of treatment. J. P. Bates (Jour. of Trop. Med. and Hyg., Aug. 15, 1913).

In *post-malarial anemias*, the prognosis depends upon the gravity of the anemia and its susceptibility to treatment. Except in those cases in which the blood impoverishment follows the pernicious infections, it is generally fair. In the latter type, death is often not far distant.

In *malarial cachexia*, a guarded prognosis should always be given, unless the patient is able to change his place of residence. In a suitable climate, under proper treatment, the prognosis is good.

PROPHYLAXIS.—The work of the United States Army Sanitation Corps in the Panama Canal Zone has demonstrated what can be accomplished. The methods necessary are thus stated: 1. **Measures** directed against the development of the plasmodia in man and in mosquitoes. 2. Measures aimed at the destruction of the malaria-transmitting mosquito. 3. Prevention of the access of the mosquito to man; both to man the infected, and man the infector. 4. **General education of the public.**

1. To destroy the source of infection in man (the gametes) **quinine** systematically employed is all-sufficient.

From 5 to 10 grains (0.3 to 0.6 Gm.) of a readily soluble salt should

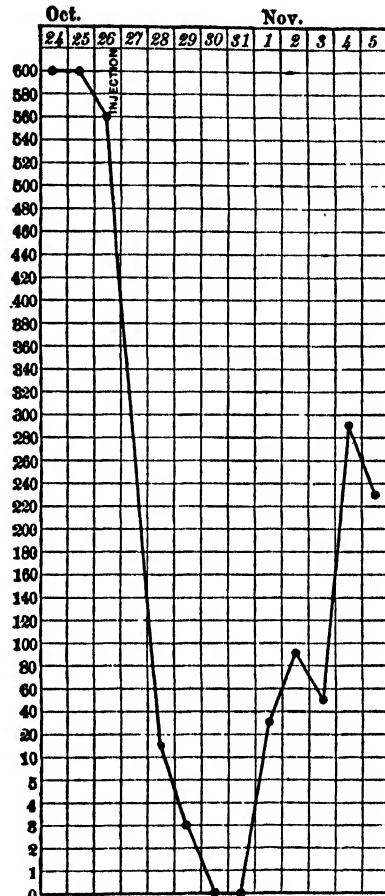


CHART VI.—Showing disappearance and reappearance of organisms after the injection of 1 Gm. of quinine and urea hydrochloride. (Case of H. J.)

be taken daily—preferably, in case of the larger quantity, in two doses, morning and noon. In certain regions, larger doses may be needed occasionally.

As Seale Harris has emphasized, malaria is perpetuated by patients carrying the plasmodium through the winter and infecting anopheles mosquitoes in the spring. Un-

cured malaria is therefore a menace to the community. The use of **quinine** should be continued until after the mosquitoes have been destroyed by the cold, while prophylactic doses should be taken the following spring.

As a factor in malaria control, malaria in infected persons may be eradicated either by destroying the mosquitoes or by destroying the infection in man. Physicians relieve their patients of active clinical symptoms, but few actually disinfect their

than 90 per cent. of patients. Bass (Jour. Amer. Med. Assoc., Nov. 22, 1919).

In studying the treatment of general paralysis by malaria inoculation, the following facts were observed in regard to quinine prophylaxis: Where inoculation was carried out with infected mosquitoes, even large doses of **quinine** given before inoculation failed to protect unless they were continued for a considerable time after inoculation; on the other hand, even small daily doses (5 grains), when continued for 2 to 6

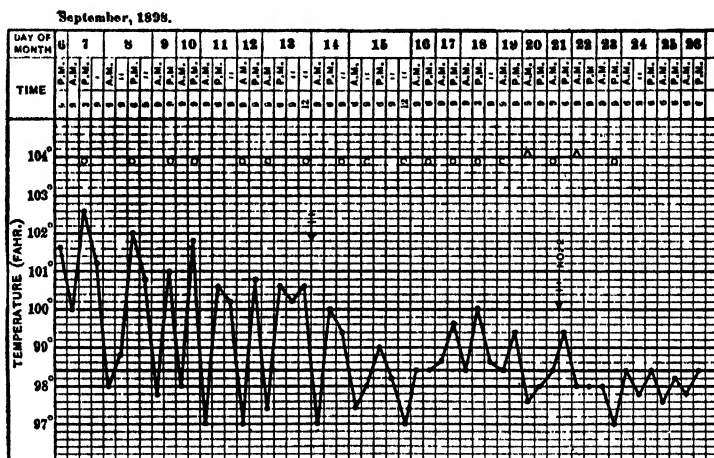


CHART VII (Illustrating diagnosis).—Mixed infection; typhoid and malaria. Widal reaction positive. Rose spots. (X, Y, Z.; from Tampa, Fla.) J Quinine and urea hydrochloride injected. O No organisms found. Δ Organisms found.

patients. In the experiments in Mississippi, the data obtained indicate that between 50.77 and 68.86 per cent. of all persons who have attacks of malaria during a given year have relapses and not new infections. The standard, practical method of treating and disinfecting persons who have malaria, adopted in the Mississippi experiments, is: Under 1 year of age, $\frac{1}{2}$ grain (0.03 Gm.) of **quinine**; 1 year, 1 grain (0.065 Gm.); 2 years, 2 grains (0.13 Gm.); 3 and 4 years, 3 grains (0.2 Gm.); 5, 6 and 7 years, 4 grains (0.26 Gm.); 8, 9 and 10 years, 6 grains (0.4 Gm.); 11, 12, 13 and 14 years, 8 grains (0.5 Gm.); 15 years and older, 10 grains (0.65 Gm.); to be taken every night. This treatment appears to disinfect more

weeks after inoculation, gave protection. Giving quinine before infection is useless. Its administration must be continued at least 10 days after the infecting feed to prevent infection from developing. The size of the daily dose given has but little influence, except that with very large doses (30 grains) the period of administration required to prevent development of infection is slightly shortened. Evidently, quinine has little, if any, action on sporozoites, and the mechanism by which development of infection is prevented is similar to that by which a cure is effected. W. Yorke and J. W. S. Macfie (Lancet, May 17, 1924).

Study of the preventive action of **quinine** in latent malaria. From 0.1 to 0.4 Gm. ($1\frac{1}{2}$ to 6 grains) of the drug

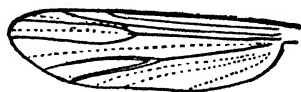
FIELD IDENTIFICATION OF MALARIA-CARRYING MOSQUITOES.

In a supplement (No. 32) to the U. S. Public Health Reports of October 19th, 1917, Surgeon Ernest E. Sweet publishes the following data for the field identification of the commoner Anopheles mosquitoes:—

For use in the field a small hand lens, magnifying from 2 to 4 diameters, is of service. Mosquitoes are distinguished from other similar appearing insects by the fringe of scales along the posterior border of their single pair of wings, the wing veins being also fringed with scales. If the insect in hand lacks the posterior fringe of scales it does not belong to the mosquito family, however much it may resemble that insect in appearance. There are three families of insects, the sand flies, the crane flies, and the midge flies, which may be confused with mosquitoes, but ordinarily the health officer will encounter little difficulty in making the differentiation even without examining the wing structure. The sand flies of the United States are much smaller in size than mosquitoes, while the crane flies are not only larger, but the body is long and slender and the length of the legs such as to be out of proportion even to that of the body. Midge flies, often called "midges," are usually seen in dancing clouds hovering over one's head in the late afternoon, and nearly all of those found in this country lack the long proboscis or biting part, have bare wings, and are more delicate than mosquitoes.



Wing of *Culex pungens*—Berkeley, 1902, Laboratory work with mosquitoes, p. 35, Fig. 27.



Wing of Diptera mistaken for mosquito—F. V. Theobald, Vol. 1, 1901, p. 92, Fig. 23.

Some species of *Anopheles* mosquitoes may fly a mile or more, but such long flights are unusual. Other varieties of mosquitoes are frequently carried several miles by the wind, but visitations of insects in this manner are not followed by outbreaks of malaria, as the insects are never Anophelines. The mosquito can not infect a person with malaria until at least eight days after it has bitten an individual with the malarial parasite in his blood, but once a mosquito is infected she probably remains so throughout life. Mosquitoes may live five or more months. The life cycle of the *Anopheles* mosquito includes four stages, the first three of which (egg, larva, and pupa) are invariably passed in water.

Determination of Sex.—Only the female bites, and for this reason it is essential that the sexes be differentiated. Fortunately this can be easily accomplished.



Head of *Anopheles*—male.

MALE.

Antennæ, of all varieties, markedly plumose, i.e., "heavily haired."



Head of *Anopheles*—female.

FEMALE.

Antennæ, of all varieties, not plumose, i.e., "sparsely haired."

Determination of Genus.—After determining that the insect in question is a mosquito and that the specimen is a female, the next step is to decide whether or not it is an Anopheline. In making this decision there are many facts to guide us, each of which must be considered in turn. For the purpose of comparison the most common variety of mosquito, the *Culex*, is selected and the differences throughout the various stages of development, beginning with the egg, noted.

Eggs.

ANOPHELES.

The eggs are laid singly, and for this reason are seldom found in nature. They float on the surface of the water and are supported by lateral air spaces.

CULEX.

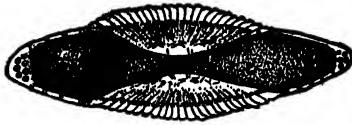
The eggs are laid in rafts or boatlike masses of about 200 and are readily visible to the naked eye. Instead of floating on the side they are arranged vertically. There are no lateral air spaces.



Ova—*Anopheles*.



Egg raft—*Culex*.



Egg—*Anopheles maculipennis*.

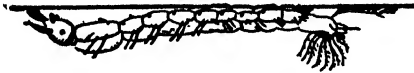


Egg—*Culex*.

Larvæ.

ANOPHELES.

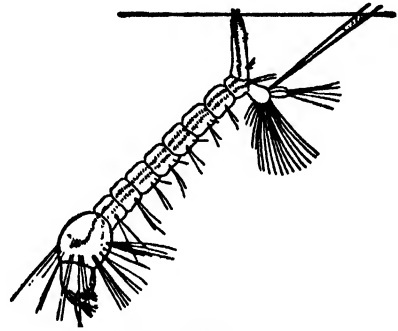
The larvæ lie at the top of the water and parallel to the surface, as Carter so aptly expresses it, "for all the world like a basking pike." The head is much smaller than the thorax. There is no respiratory siphon. Upon being frightened the larvæ may dive, but usually they dart parallel to the surface.



Larva of *Anopheles*.

CULEX.

The larvæ hang head downward from the surface of the water at an angle of about 60°. The head is much larger than the thorax. There is a long respiratory siphon at the tail. Upon being frightened the larvæ usually dart downward.



Larva of *Culex*.

Pupæ.

ANOPHELES.

The pupæ are larger in the anteroposterior direction and narrow laterally. The respiratory siphons are short and trumpet like, the small end being attached near the middle of the thorax.



Anopheles punctipennis—Say, (Mosquitoes of N. America, Vol. 2, 1912, Howard, Dyar, and Knob plates.)

CULEX.

The pupæ are shorter and broader from side to side. The respiratory siphons are long, narrow, and tube like and are attached near the posterior end of the thorax.



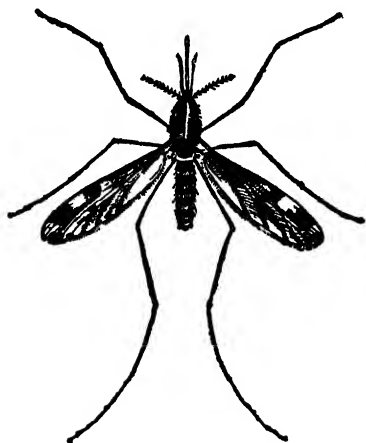
Culex pipiens—Linnaeus. (Mosquitoes of N. America, Vol. 2, 1912, Howard, Dyar, and Knob plates.)

It should be borne in mind in searching for larvæ that they are remarkably shy, and for this reason it may be necessary for the examiner to wait over the pool for some little time in order that they may come to the surface after their disappearance. Should the observer encounter difficulty in determining the genus of the aquatic forms he should remove the larger larvæ or pupæ from the pool and allow them to hatch under artificial conditions, in this way obtaining the adult insect for additional guidance. While the larval characteristics are thoroughly dependable in the determination of the *Anopheles* genus, the health officer will naturally be called upon more often to make the identification from the adult specimen; for this reason familiarity with the appearance of the fully developed insect is all important. Adult *Anophelines* are distinguished by the following characteristics:

Adults,

ANOPHELES.

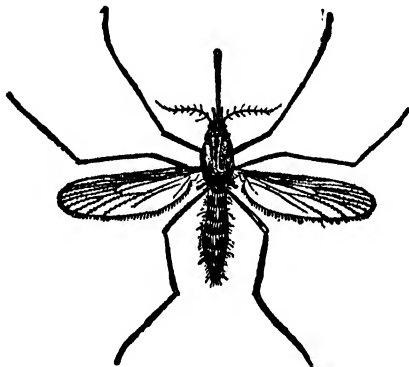
The wings are distinctly spotted. In the female the palpi are about the same length as the proboscis. This is true in no other mosquito except one, which happens to have a curved proboscis. Therefore, if the specimen is a female and if the palpi are nearly as long as the straight proboscis the insect is an *Anopheles*.



Anopheles punctipennis, female.

CULEX.

The wings are not spotted. In the female the palpi are much shorter than the proboscis.



Culex pipiens, female.

When resting or biting the proboscis, head, thorax, and abdomen form one straight line.

When resting or biting the insect is "humpbacked"; head and abdomen are down, thorax is up.

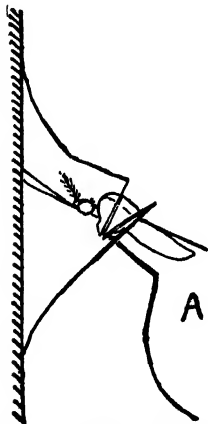
Habits.

ANOPHELES.

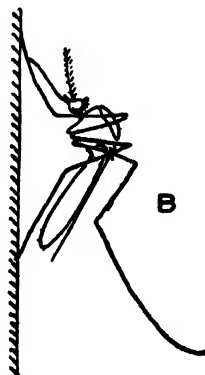
The *Anopheles* mosquito is far less annoying than the *Culex*. It seldom bites in the daytime and does not often attack a person moving about. The bite is also less painful. The hum of the insect is not as distinct as that of the *Culex*. *Anophelines* prefer to breed in cleaner water than do the *Culicines*.

CULEX.

The *Culex* mosquito is distinctly annoying. It bites at all times and is not shy, as is the *Anopheles*. The bite is irritating. The hum is particularly loud. *Culicines* are less particular concerning the character of the water in which they breed than are the *Anophelines*.



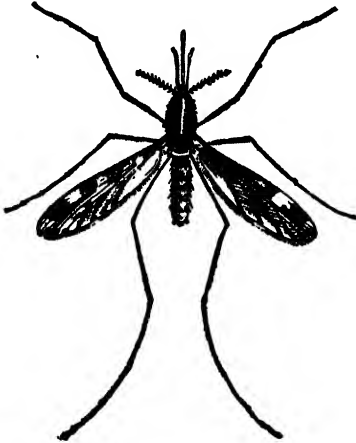
Resting position—*Anopheles*.



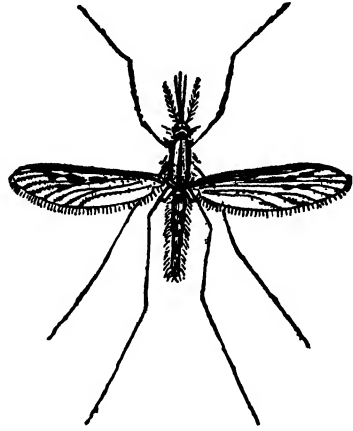
Resting position—*Culex*.

Three Anophelines occur commonly in the United States. All have been proven to be transmitters of malaria. They may be distinguished by their wing markings as follows:

Anopheles Punctipennis.—A large square or oblong white or yellowish patch at the anterior margin of the wings near the outer end is the striking characteristic. This patch of white is readily visible to the naked eye and is easily seen even when the insect is in the resting position with the wings crossed. After determining that the insect is a female *Anopheles* this patch of white should be looked for; if not found the specimen is sure not to be a *punctipennis*. The anterior margin of the wing is dark, while the balance is lightly spotted or mottled with black, with an almost invisible white spot at the extreme apex. Besides breeding in quiet waters *A. punctipennis* is the only one of the three *Anophelines* which breeds in running water and streams which are subject to freshet from rains. This particular insect is more often found on porches, in outbuildings, and under houses than within habitations.



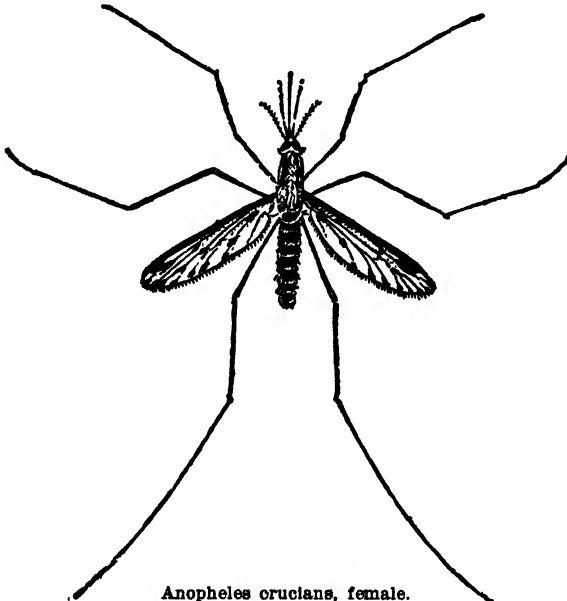
Anopheles punctipennis, female.



Anopheles quadrimaculatus, female.

Anopheles Quadrimaculatus (maculipennis).—Three to five, but usually four, black spots (patches of black scales) on the second and fourth wing veins. Breeds more often in quiet waters, pools, etc., and invades human habitations.

Anopheles Crucians.—The wing is dusky and the veins are prominently marked. The characteristic marks are three small spots of black on the sixth wing vein (thoracic end, posterior margin). In the young insect the spots are apt to be distinct, but if the specimen is old the end spot is usually missing.



Anopheles crucians, female.

was given daily for 6 months to 70 children in Algeria, all carriers of malarial parasites. Complete disappearance of *Plasmodium praecox* (*falciparum*) was obtained, while in a few instances *P. vivax* persisted. The parasite index as a whole decreased from 53 to 11 per cent. Foley and Brouard (C. r. Soc. de biol., Apr. 3, 1925).

2. To destroy the mosquito and prevent breeding, it is necessary to institute thorough and free **drainage of marshy lands**, swamps, and known breeding places. **Kerosene oil** spread over the surface of the water will destroy the larvæ. A mixture containing **crude carbolic acid** is also employed. **Aniline dyes**, as advocated by Celli, deserve further investigation and trial. **Pyrethrum powder** may be burned on porches, in chambers, and other places frequented by the insects. The effectiveness of **fish** in checking the breeding of malarial mosquitoes has been demonstrated in recent years. Other methods can be found in special works upon this subject.

The writer applies the principle of **sticky fly paper** to the destruction of malaria-bearing mosquitoes. A kind of screen or trellis work, about 6 feet by 4.5 feet, is smeared thick with heavy crude oil, which is sticky enough to catch and hold mosquitoes. They can be attracted to the screens by hanging a small lantern in the center. Bosurgi (Gaz. degli Osped., vol. xxviii, Nos. 21-27, 1907).

To prevent mosquitoes from biting, the writer found a **phenol lotion**, 1:60 or 1:40, and also **eucalyptol**, f3j (4 c.c.), in glycerin or olive oil, f3ij (60 c.c.), useful for local application. G. A. Wolfendale (Jour. of Trop. Med. and Hyg., May 2, 1910).

Mosquitoes will not bite where the skin is smeared with **petrolatum**. The writer smears all the exposed skin with petrolatum once every day or two, and found that this permits tran-

quil sleep amid myriads of mosquitoes. Albano (Policlinico, Sept. 1, 1918).

Stock raising tends to divert the mosquitoes away from man. The writer advises the keeping of large stocks of cattle or other animals in addition to **draining** and **screening**. Grassi (Ann. d'ig., June, 1922).

In malarial control studies in Nicaragua, **fish** were relied on exclusively to control anopheles breeding in natural streams and ditches dug for drainage purposes. With a reasonable amount of care in keeping ditches and laterals open, the degree of control secured was surprising. All ponds were dried and all pools either drained or filled. Molloy (Amer. Jour. of Trop. Med., Mar., 1924).

3. Exclusion of the mosquito requires effective **screening** of all dwellings, and mosquito **canopies** over the bed. One should **sleep** at a sufficient height **above the ground**, and **dwellings** should be located as far as possible from **marshes** and **mosquito-harboring vegetation**.

Mosquitoes will enter a house in search of blood, as this food accelerates ovulation. They usually find entrance through defective screens, such as those of 12 or 14 mesh wire; corroded or torn wire screens, or the sides of poorly-fitting screen doors and window screens. They also enter through chimneys, drain holes, etc. Anopheles mosquitoes usually take their flight during the hours between sunset and sunrise. They are attracted to houses by light. They are not content on finding that the entrance to a house is closed to them by screens, but seek to find any opening by which they can enter. It is therefore important that every accessible opening be carefully closed.

It is very generally accepted that the anopheles mosquitoes do not fly high, and therefore do not enter rooms on the second or third floors of a house; but it has also been found that these mosquitoes will fly over the

tops of houses and, when attracted by the reflected light from chimneys, will enter by that route through the fire-places into the house. R. H. von Ezdorf (U. S. Public Health Service Reports, Feb. 27, 1914).

Quinine prophylaxis failed to prove its value during the World War and must be ruled out as a routine measure to be solely depended on for armies in active service. The writer advocates **mosquito nets** and strict rules for their adequate use. Besides these, mutual co-operation to brush mosquitoes from hands and face is urged. Officers and nurses must protect their ankles by **thick hose or mosquito boots**. **Gauntlets** and **face nets** should be worn by pickets and nurses, and **repellants** should be applied at frequent intervals—every 2 hours. Each morning every man must search the dark places in connection with his bivouac for resting mosquitoes. In addition, 1 man per company should be permanently employed in going around these places trying to find mosquitoes that have been overlooked. The **cutting of scrub** for 200 yards around camps which are to be occupied for any length of time and the **treatment of collections of water** in the vicinity should be undertaken by the sanitary squad. Boyd (Jour. Roy. Army Med. Corps, Sept., 1924).

During the World War, the Bulgarian army being deprived of quinine in 1918, combating of mosquitoes was resorted to by all. There was less malaria than in the preceding year when quinine had been available. The **mosquito net**, if good, is the best personal protection. Muehlens (An. de la Fac. de Med., Lima, Dec., 1924).

Anopheles that gain access to screened buildings can be found on the screen in the early morning and again at dusk, at which times it is easy to destroy them. Even in unscreened buildings the gorged anopheles resting on the walls are easy to kill during the daytime with a fly swatter; when the family is interested, they destroy nearly all the potentially infected anopheles. Many anopheles will des-

troy themselves in **mosquito traps**, which provide daytime resting-places protected from bright light and air currents and are treated with cheap tanglefoot compounds. Boxes placed bottom upward, with one side removed, are desirable collecting places for *A. quadrimaculatus*, and may be placed in the shade near potential breeding places and wet areas. Anopheles readily devour small floating particles of **Paris green**, and a dust cloud containing 1 per cent of Paris green effectively controls anopheles production in bodies of water with much aquatic vegetation, without harming the fish or other aquatic life. J. A. Le Prince (Proc. Internat. Conf. on Health Probl. in Trop. Amer., 1924).

4. Campaigns of **public education** have been carried on, and should be further encouraged. Much can be done in this manner by driving home to the public the tremendous economic loss due to malaria.

Isolation of malarial sufferers is recommended in camps and similar places.

TREATMENT.—In every case in which acute malaria is suspected, the patient should be put to **bed** and carefully observed. The **nursing** and **diet** should be such as are appropriate in fevers in general, until typhoid, at least, can be excluded, when the diet may be made more liberal. **Calomel**, followed by a mild **saline aperient**, should be administered; and after the resultant evacuation, the **bowel** should be **irrigated** with a warm saline solution. **Disinfectant measures** appropriate to typhoid should be instituted and kept up until proved to be needless.

The medicinal treatment of acute malaria may be summed up in a word—**cinchona**. The bark and its derivatives should be, if possible, used in every case, both as a cura-

tive agent and as a means of prophylaxis.

There are a few instances in which the cinchona group of remedies cannot be employed in effective dosage on account of hypersensibility of the individual patient; and there are some instances in which these drugs are ineffective for reasons not apparent. But both classes of exceptions are numerically insignificant in comparison with the thousands of cases in which the rule applies. They will be discussed later.

According to Paine, a hypodermic injection of **morphine sulphate**, $\frac{1}{4}$ grain (0.016 Gm.), and **atropine sulphate**, $\frac{1}{150}$ grain (0.0004 Gm.), will markedly modify the severity of the chill if administered before it is due.

We have now to consider in relation to the great bulk of cases—*i.e.*, those in which cinchona is tolerated and is efficacious: 1. The effect of the drug. 2. The choice of preparation. 3. The manner of administration. 4. The time and frequency of administration. 5. The dose. 6. Possible contraindications.

No dosage of **quinine**, even if continued daily for periods up to 2 months or more, will absolutely preclude relapses. No single dose of quinine can destroy more than, say, 20 per cent. of the asexual parasites actually present in the patient on the day of administration. If the next day's dose kills the same proportion of the remaining parasites, and so on day by day, then, by a simple calculation, one infers that this dosage must be continued daily for about 3 months before the infection is extirpated entirely.

The writer recommends, and uses for his own private patients, the following treatment for men: 10 grains (0.6 Gm.) of **quinine sulphate**, **hydrochloride** or **dihydrochloride**, preferably in solution, once a day just before breakfast every morning for 3 months.

The patient becomes accustomed to this after a few doses, and the following meal takes the taste of the medicine out of his mouth. To the few persons who complain of indigestion or vomiting the same doses may be given in tablet or capsule. The writer cured his own malaria in 1897 with this prescription taken for four months, without any relapse. If relapses do occur, it is generally within the first 3 weeks; they should be treated with an additional similar dose before dinner on days when the temperature is above normal, and for 3 or more days longer, after which the single daily dose is resumed (smaller doses for women and children). The bowels are to be kept regular, preferably with a dose of **liquid petrolatum** at bedtime, and a **glycerin suppository** every morning on waking, if necessary. Many physicians recommend much shorter courses of treatment, but this probably means a greater risk of relapse after the end of the course, and if a relapse does occur the whole course must be taken over again. If the patient rebels after a month's treatment, he should be warned that relapses are likely to occur as long as a single parasite exists in his blood.

Intramuscular injections of 15 grains may be employed at first for obstinate, refractory, dyspeptic, or serious cases, but they have no advantage for parasitocidal purposes over the oral doses, and sometimes cause local mischief. Intravenous injections have perhaps a little higher parasitocidal index than the other routes; but three out of ten cases relapsed after 10 injections on ten consecutive days each, and they are seldom used except for very serious or sudden cases. **Rest in bed**, **iron**, **arsenic**, and **alcohol** may be given when indicated, **morphine** for severe rigors, and **diaphoretics** at the height of the fever. Sir Ronald Ross (*Practitioner*, Nov., 1925).

Action of Cinchona.—Cinchona contains a number of alkaloids of which quinine is the most potent and this, in the form of one of its salts, is the anti-

malarial specific *par excellence*. Notwithstanding its large use and careful study, its mode of action upon the infecting organism and upon the blood has not been so clearly demonstrated as to escape question.

Certain observers hold that the blood plasma and the phagocytes are the actual efficient agents in the destruction of the malarial organisms. They point to the fact that it is the free spores (merozoites) and the young organism rather than the adult hemozobas which apparently yield to the drug, and credit quinine only with a hemolytic effect upon the infected corpuscles, which permits the plasma to reach the merozoites at their least resistant period. From the clinical side they cite the inability of quinine given before an attack to abort the paroxysm and the relative meagerness of organisms after a hemolytic crisis, as in black-water fever. From the experimental side they bring forward observations such as those of Bass, who has cultivated the plasmodia *in vitro*, studying carefully the effect of serum alone, and of quinine and other substances under conditions which permitted or excluded the serum action.

Nevertheless, the great outstanding fact remains that it is just quinine (or some recognized parasiticide, such as salvarsan) that cures malaria. (The writers are skeptical of so-called spontaneous recovery.) The blood plasma and the phagocytes alone do not prevent original infection; they do not even prevent the few spores that ordinarily survive quinine, from developing, multiplying, and producing relapse—perhaps through Craig's intracorpuseular conjugation—in cases inadequately treated; they do not prevent or overcome latent, chronic, or masked

infection. On the other hand, quinine, if supplied to the blood continuously and sufficiently, enables one to resist inoculation by infected mosquitoes; prevents relapse; and if administered *at the proper time, and in the right way*, will prevent an expected paroxysm from manifesting itself. There seems to be little ground, therefore,—while admitting the value of serum and phagocyte,—for questioning the actual parasitidal effect of the drug.

In the case of the ordinary *tertian* organism (*Hæmaphys vivax*) quinine is toxic to all stages of the developing parasite, until the beginning of sporulation, causing fragmentation and degeneration. It is particularly fatal to the young plasmodia and to the spores when set free. Schso has shown that it will inhibit the development of gametes within the mosquito.

According to Craig, quinine is likewise toxic to all stages of the *quartan* parasite (*Hæmaphys malariae*) although the latter is more resistant than the *H. vivax*. Antolisei and Golgi, however, found quinine without effect upon the adult quartan parasite. The senior writer's limited (clinical) observations accord rather with those of Craig. Data are wanting to determine the effect of quinine upon quartan gametes.

Marchiafava and Bignami have carefully studied the effect of quinine upon *estivoautumnal parasites*. They found that in fresh specimens the young plasmodia became discoid and were extruded from the erythrocyte, while their mobility remained normal or was increased. Craig, however, was not able to observe this extrusion, although he saw change of form and position. The drug has little effect on the larger pigmented forms, the only change de-

monstrable being an increase in the refractive index. Degeneration by fragmentation has not been observed in unstained specimens.

These pigmented forms can continue their development with slight morphologic changes for as long as three days after quinine has been administered, but ultimately succumb to degeneration, such as has been described in the ordinary tertian parasite. The

vented by the timely and persistent use of quinine.

Bass contends that quinine has no direct destructive effect upon malarial organisms, its virtue depending upon the fact that it renders the red blood-cell protecting the parasite more permeable to the all-sufficient serum. Hence the drug can bring about the destruction of those parasites that are in the circulating blood, but not of those

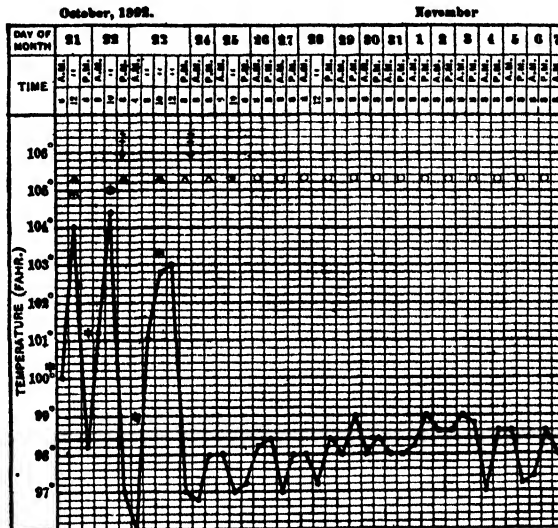


CHART VIII.—Double tertian intermittent of 30 days' duration prior to treatment. Two injections. Recovery. (John S.; Autumn, 1892.) * Beginning of chill. ⊕ End of chill. ‡ Injection of 1 Gm. of quinine and urea hydrochloride. Δ Organisms, pigmented, numerous. △ Organisms, pigmented, few. ○ Organisms, hyaline, few. ○ No organisms.

ring forms show slight degenerative changes, especially loss of nuclear chromatin. The young pigmented forms quickly undergo fragmentation. The gametes (crescents) are highly resistant and quinine does not appear to hinder their capacity to develop within the mosquito. Their appearance, however, may be prevented if quinine be administered promptly and adequately at the beginning of an infection.

Intracorpuseular conjugation, which tends to keep infection alive and bring about relapses, is absolutely pre-

contained in corpuscles that have become lodged in the deeper capillaries, which are not reached by it until they segment. His experiments *in vitro* show, moreover, that blood from individuals fasting and at rest is more destructive to the organisms than that taken during exertion or after a meal; but that this superiority of fasting blood can be overcome, and the cultures protected, by the addition of a certain quantity of dextrose. Hence it would appear that the empirical rule of administering quinine "upon an empty

stomach" is well founded, and that it might be well to go still further and prolong the fast until after the time of paroxysm. The importance of rest is also emphasized by these studies.

Choice of Preparation.—Since cinchona alkaloids have been available, the bark and its galenical preparations have fallen into disuse for the treatment of active malaria, but they may be used in after treatment, especially in the form of the compound (Huxham's) tincture, for the sake of the tonic effect of the pleasant bitter upon the digestion and appetite of the patient.

In ordinary tertian infections it is of little moment which of the **quinine salts** is used; but in estivo-autumnal infections, and especially in the pernicious varieties, and also in highly malarious regions, promptitude of action and potency of effect are important, and small differences become great. In the senior writer's experience the very soluble double salt, somewhat loosely termed **quinine and urea hydrochloride** has proved the most efficacious. This may be owing in part to a superior cytolytic power.

As little as 0.5 Gm. ($7\frac{1}{2}$ grains) of **quinine hydrochloride**, given with 0.05 to 0.1 Gm. ($\frac{3}{4}$ to $1\frac{1}{2}$ grains) of **arrhenal**, will cure the most rebellious forms. The 2 drugs should enter the blood together in 6 or 7 doses before a paroxysm. The arsenical reinforces quinine and probably activates phagocytosis. A. Gautier (Bull. de l'Acad. de méd., Apr. 24, 1917).

In general, the question is one of (1) the solubility, and (2) the alkaloidal richness, of the particular salt. The following table will prove useful to show these points:—

Salt.	Percentage of alkaloid in salt.	Solubility in cold water. (Expressed in parts by weight of solvent to 1 part of drug.)
Sulphate	73.5	800
Bisulphate ..	59.1	11
Hydrochloride	81.8	40
Dihydrochloride	72.0	0.96
Carbamide-hydrochloride.	58.0	1
Hydrobromide	76.6	45
Dihydrobromide	60.0	7
Phosphate	76.2	420
Valerianate	73.0	120
Lactate	78.2	10
Salicylate	70.1	225
Arsenate	69.4	Very slight.
Tannate	20.0	Very slight.

Methods of Administration.—Quinine can be given by the mouth or the rectum, or may be injected into the veins, into the muscles, or under the skin. The writers prefer the hypodermic or intramuscular method, when the injections are made by one who is familiar with the technique that safeguards the patient from sloughing or abscess. In hospitals, as a rule, this should be the duty of internes, not leaving it to nurses, save in the exceptional instance.

Quinine salts can be administered efficaciously *by the mouth*, but should always be given in such form that the drug can be absorbed readily from the stomach. Solution, wafer, or dry capsule may be given, according to convenience and eligibility in the individual case. Pills and tablets are to be avoided. The drug is most effective when taken into a fasting stomach, and after free purgation—hence meal-times and stools should be adjusted to the necessities of the case. *Rectal administration* is not a method of choice, but may be employed when absolutely necessary. Large doses are requisite, at least double the quantity that would be given *per os*.

Solution or suppository can be used, preferably the latter. Absorption is slow in any event, and solutions sometimes irritate. The anesthetic effect of the combination with urea is here, at times, of service.

For *hypodermic* and *intramuscular injections* the preferable salts are the *dihydrochloride*, *chlorhydrosulphate*, and the *carbamide hydrochloride* (quinine and urea) combination; although the hydrochloride, the bisulphate, the acid hydrobromide, and even, in emergency, the sulphate have been employed.

The technique of the senior writer is absolutely necessary with the carbamide hydrochloride combination (quinine and urea hydrochloride) and may be of benefit with the other salts. The skin at the site of injection is to be cleansed thoroughly (*e.g.*, with green soap and alcohol) and painted, for an area of about 1 inch in diameter, with tincture of iodine or iodine-acetone. The syringe and needle should be surgically sterilized; and, preferably, an all-glass high power syringe used. The needle is to be plunged deeply beneath the iodized skin, and best, into the muscle. It should be emptied completely before withdrawal, to avoid dripping upon the skin. As a further precaution, a piece of thin rubber protective may be stretched over the skin and the needle passed through it to make the injection—but this is not essential. The point of puncture should be sealed with collodion or iodoform-collodion. The solution to be injected should be made extemporaneously with boiling water. A convenient custom is to have a supply of papers or capsules, each containing the weighed quantity for

a single dose (usually 1 Gm.—15.5 grains) in the ward, and it is then a simple and quick matter to fill the syringe with the hot water and dissolve the drug in this quantity—ordinarily 2 or 3 c.c. A gram (15.5 grains) of quinine dihydrochloride, or of quinine and urea hydrochloride, will dissolve, however, in 1 c.c. of water.

The superiority of **quinine and urea hydrochloride** for injections lies in its high solubility. An ordinary syringe-ful may thus be made to contain from 15 to 18 grains (1 to 1.2 Gm.) if necessary. The preferable solution is 50 per cent., and the ordinary dose is 1 Gm. (15 grains) in 2 c.c. ($\frac{1}{2}$ fluidram) of water. In malaria of the types ordinarily seen in northern latitudes, a single such injection will cause suspension of the paroxysms for from a week to a fortnight ($6\frac{1}{2}$ to $13\frac{1}{2}$ days). One injection daily or on alternate days for a week ordinarily suffice to bring about complete recovery. After this, to make sure against chronic infection or sequels, the drug should be continued in doses of 10 grains (0.6 Gm.) in capsule by the mouth, daily, for another week; and then administered once a week, in the same way, for two or three months. S. Solis-Cohen (Med. Times, Mar., 1912).

The following plan of treatment practically rid Americans of relapsing malaria in the Canal Zone:—

(1) **Calomel**, 3 to 5 grains (0.2 to 0.3 Gm.), followed in twelve hours by 2 fluidounces (60 c.c.) of 50 per cent. **magnesium sulphate** solution. (2) **Quinine sulphate**, 20 grains (1.25 Gm.) in 4 fluidrams (16 c.c.) of distilled water with 4 drops of concentrated **hydrochloric acid**. (3) **Quinine sulphate**, 15 grains (1 Gm.), prepared as before, three times daily for a week, after which dose reduced to 30 grains (2 Gm.) daily for ten days. (4) When vomiting is present, **quinine dihydrochloride**, $22\frac{1}{2}$ grains (1.5 Gm.), given in 5 fluidrams (20 c.c.) of normal **salt solution** as deep subcutaneous injection.

tion. (5) In obstinate relapsing cases, **quinine injections** of 15 to 30 grains (1 to 2 Gm.) in 300 to 500 c.c. (10 to 16 fluidounces) of normal saline, given **intravenously** on two succeeding days, then 45 grains (3 Gm.) a day by mouth. (6) **Arsenic, iron, and strychnine** as tonics. James (Jour. of Infect. Dis., May, 1913).

Ochsner's **intermittent quinine treatment**, possibly with the interpolation of **neosalvarsan** injections, has won wide acceptance for the treatment and prophylaxis of malaria. It prevents quinine habit and distributes the quinine doses so as to assure sufficiency of quinine in the organism at every stage of development of the plasmodium. It is advisable to give the quinine in solution, or in powder form followed by a drink of very dilute hydrochloric acid. Ochsner first gives a **purgative** and then a **liquid diet** with rice and vegetables. Every 2 hours for 2 days, 0.15 Gm. ($2\frac{1}{4}$ grains) of quinine is given, with 250 c.c. ($\frac{1}{2}$ pint) of hot tea, and every 3 hours for 5 days small doses of **arsenic**. On the 8th day a **purgative** is given, followed on the next 2 days by 0.15 Gm. of quinine and hot tea every 2 hours, and then a **tonic** for some weeks. Hajos (Orvosi hetil., Apr. 13, 1924).

Intravenous injection is urged by many authors, especially Baccelli, Marchiafava, and Bignami, for selected cases, and whenever there is urgency, as in the comatose, algid, and other pernicious forms.

Baccelli's solution has about the following formula:—

R *Quinine dihydrochloride* gr. xv (1 Gm.).
Sodium chloride. gr. iss (0.075 Gm.).
Distilled water .. f3iiss or f3iij (10 c.c.).

Under aseptic precautions, this method has, according to Baccelli, reduced the mortality of pernicious forms of malaria to 6 per cent.

The vast majority of malarial cases yield within 5 to 7 days to quinine by

mouth in doses of 30 grains (2 Gm.) a day. In the more serious infections, intravenous injections are more effective than intramuscular, and are safe if given slowly. A method which seems largely to obviate the disadvantages of both intravenous and intramuscular injections of quinine is the substitution of **cinchonine dihydrochloride** for the quinine. This, when given intramuscularly, is absorbed much more rapidly than the quinine salt, as shown by symptoms of cinchonism often appearing within $\frac{1}{2}$ hour, which the author has never seen after quinine injections. Also, far less pain and induration is induced by the cinchonine salt. Most of the cases thus treated were benign tertian. The dosage is 10 to 15 grains (0.6 to 1 Gm.) in $1\frac{1}{2}$ to 2 c.c. (24 to 32 minims) of fluid, injected into the deltoid once daily on 4 consecutive days, after which time bilious remittent cases yield, and quinine can be continued orally. Sir Leonard Rogers (Proc. Internat. Conf. on Health Probl. in Trop. Amer., 1924).

Time and Frequency of Administration.—In cases of pernicious type, or of great severity, quinine should be given intravenously, intramuscularly, or hypodermically as soon as the diagnosis is made—in urgent cases, even before the microscopic study of the blood, since this may be completed while the drug is at work, and in any event no harm will be done. An unnecessary dose of quinine will not kill—pernicious malaria may. Repetition of the dose should also be more frequent than in ordinary cases—every two to eight hours, according to effects. Ordinarily, however, it is safe to wait and establish by clinical observation and microscopic blood studies the species of the infecting organism and the type of the paroxysms. Since quinine action is at its height about one

to two hours after intravenous injection, three to four hours after intramuscular or subcutaneous injection, and six to eight hours after ingestion, the drug should be administered accordingly—so that its period of maximum effect may coincide with, or slightly anticipate, the period of complete segmentation of the parasite—the aim being to kill the spores and young organisms and thus prevent them from reaching maturity to provoke further paroxysms and to bring about further intoxication and cell destruction. Thus, if the next paroxysm is expected at, say 4 o'clock P.M., the intravenous injection should be made one hour earlier (*i.e.*, at 3 P.M.) or the intramuscular injection four hours earlier (*i.e.*, at noon), the entire daily dose (about 1 Gm.—15.5 grains) being given. If the drug is to be taken by the mouth, the daily dose (about 1.5 Gm.—24 grains) is best divided into two portions, of which one—in the case supposed—would be administered at 12 M. and one at 8 A.M. (four hours and eight hours, respectively, before the expected chill). If the paroxysms tend to recur daily, the drug should be given daily in the same way (adjusted, however, to the so-called *anticipating* chill time—*i.e.*, one hour earlier each day) or to the actual variation of period established by observation, which may be, as in cases observed by the writers, twenty-one and twenty-four hours alternately, or some other figure. When the paroxysms are *tertian*, only a half-dose of quinine need be given on the free day, and then at any convenient hour, but preferably in the morning, after a stool, and before food is taken. On the day of expected re-

turn of the paroxysm the full dose is to be given, in the same way as before. This is to be kept up for a week or two, since some of the parasites escape destruction, and in the course of a week to a fortnight multiply sufficiently to cause relapse.

In cases in which intravenous or intramuscular injection has been employed during the first few days or the first week of the attack, administration by the mouth can frequently be substituted thereafter. If the case be of remittent or subcontinuous type, the drug is best administered every four hours in doses of from 5 to 10 grains (0.3 to 0.6 Gm.) according to severity of symptoms and individual reaction to medication..

After a sufficient continuance of full treatment—according to the type and severity of the infection, and the result as shown clinically and microscopically—the dose of quinine may be reduced one-half, and this amount given daily or on alternate days, in one or two portions. This should be continued for some two to four weeks, or longer if necessary. After that, for at least three months the patient should take a full dose of quinine (not less than 15 to 20 grains in two portions) every seventh day (not every eighth day, as every Saturday or Monday, but *anticipating one day each week*, *e.g.*, Saturday, Friday, etc.). Should symptoms recur, active, full, continuous treatment should be resumed at once.

In cases of *remittent* or *subcontinuous type* the effective dose is to be repeated daily—either by a single injection, or in fractions every three or four hours,—by the mouth. A sufficient dose should be continued during and after convalescence, as already stated.

It is necessary to keep quinine in the blood for a period of at least forty-eight hours, preferably seventy-two hours or three days. Thirty grains (2 Gm.) of quinine on each of three consecutive days always destroy all asexual plasmodia in the patient. There are no exceptions. Relapses result from reproduction in some manner not now well understood of sexual plasmodia or gametes which are usually present in variable number. They reproduce in seven days and multiples of seven days, and give rise to the relapses occurring usually on the seventh, fourteenth, twenty-first, and sometimes twenty-eighth days. C. C. Bass (N. Y. Med. Jour., Jan. 10, 1914).

From 50.77 to 68.86 per cent. of the malaria occurring in a representative malaria locality of the United States including thousands of cases, was relapse and not new infection. This indicated great inefficiency of the treatment of malaria practised there.

The chief cause of ineffective treatment was the employment of spectacular and impractical methods, and the discomfort and inconvenience of quinine given by hypodermic injection or of quinine in solution. Neither method could be continued long enough to disinfect the patient. Blood examination could not be depended upon to determine when disinfection had been accomplished. The only trustworthy guide was the length of time proper quinine treatment had been kept up. An effective and practical method of treatment to disinfect the patient after the acute symptoms had been relieved was to administer 10 grains (0.66 Gm.—proportionate doses for children) of quinine sulphate every night before retiring, for a period of 8 weeks. This was effective in about 90 per cent. of cases. Where there was any reason to suspect that the case might be exceptional or one in which disinfection was more difficult to accomplish, the treatment was continued for more than 8 weeks. C. C. Bass (N. Y. Med. Jour., June 14, 1919).

Dosage.—It should be evident from what has been said that the dose of quinine in malaria, like that of any other drug in any other malady, is *enough, repeated sufficiently often*. But unlike most other drugs in most other maladies, it is better to give too much than too little. Especially is this so in the tropics and other regions where severe malaria is endemic, and *a fortiori* in the pernicious forms of the disease, or even in the milder cases of infection with crescent-forming organisms. Whether or not a given dose is sufficient can be determined only by the result. When feasible, the blood should be studied for the disappearance and reappearance of organisms, and for changes in their morphology. Otherwise clinical data must be relied on. The most important is the degree and permanence of the effect in controlling or suppressing paroxysms. Among the so-called physiologic (in reality, toxic) effects of quinine, ringing in the ears, if slight, is to be welcomed. Only that quantity of drug not used up in destruction of parasites is available for such effects; and a slight tinnitus indicates, therefore, a slight excess of the drug over the absolute necessities. Severe tinnitus or ocular symptoms of any kind, however, indicate a greater excess of drug than is desirable, and this should be corrected in subsequent doses.

In ordinary cases of *simple tertian infection* as seen in temperate climates, 1.6 Gm. (24 grains) of a fairly soluble quinine salt (*e.g.*, the hydrochloride, or the carbamide-hydrochloride combination) given *by mouth* in 2 or 3 portions in the first twenty-four hours is generally sufficient. When the paroxysms recur daily (*double tertian*) this quantity is to be repeated daily. Other-

wise 12 grains (0.8 Gm.) may be given the following day—and so on, as set forth in the previous section.

The standard treatment for the acute malarial attack advocated by the National Malaria Committee consists of 10 grains (0.6 Gm.) of **quinine sulphate** by the mouth 3 times a day for at least 3 or 4 days, followed by 10 grains once daily, before retiring, for 8 weeks. The doses for children range from $\frac{1}{2}$ grain (0.03 Gm.) below 1 year to 10 grains at 15 years or older. In subjects infected with malaria but free of acute symptoms, the 8 weeks' treatment is alone necessary.

According to Wherry, the dose of **quinine** in children should be relatively larger than in adults. He adopts the following plan: Drug given every 2 hours (4 or 5 doses daily) for 3 days, beginning when temperature is at its lowest, or in such manner that the last dose is taken 2 or 3 hours before the time of the expected paroxysm. For a 1 year child, 1 grain (0.065 Gm.) of the sulphate may be given at each dose; children of 18 months to 2½ years should have 2 grains (0.13 Gm.), and over 2½ years, from 2½ to 3 grains (0.16 to 0.2 Gm.). After the third day, if the condition of the patient is improved, the same dose is given *t. i. d.*; after several days more, $\frac{1}{2}$ the dose is given *t. i. d.* for at least 1 week more.—ED.

Attention called to the availability of **cinchonine hydrochloride** as an equivalent substitute for quinine in tertian malaria. By the mouth, not over 1.5 Gm. (23 grains) a day should be given, divided into 3 doses. W. Cordes (Arch. f. Schiffs u. Trop. Hyg., xxviii, No. 3, 1924).

In Major Sinton's treatment, in which an **alkaline mixture** is combined with **quinine**, the alkaline mixture for an adult consists of **sodium bicarbonate**, 60 grains (4 Gm.); **sodium citrate**, 40 grains (2.6 Gm.), and water, to make 1 ounce (30 c.c.). The quinine mixture consists of **quinine sulphate**, 10 grains (0.6 Gm.); **citric acid**, 30 grains (2 Gm.), and **magnesium sulphate**, 60 grains (4 Gm.), with water, to make 1 ounce.

On the first day 4 doses of the alkaline mixture and 2 of the quinine

mixture are given, the latter on each occasion 15 minutes after the alkaline mixture; for the next 4 days, 3 doses a day of the alkaline mixture, followed after 15 minutes by 3 doses of the quinine mixture, and for the next 2 days, 2 doses of the alkaline mixture, followed, after a 15 minutes' interval, by 2 doses of the quinine mixture. The patient thus takes in all during the week 180 grains of quinine sulphate. K. V. Raju (Indian Med. Gaz., May, 1925).

By the subcutaneous or intramuscular route a dose of 1 Gm. (15.5 grains) of quinine and urea hydrochloride ordinarily suffices, and if this quantity be given not longer than four hours before the expected paroxysm, or even during the chill, it is frequently sufficient to prevent recurrence either for six and one-half or thirteen days, although organisms in diminishing number may sometimes be found in the blood for two or three days after the treatment, and usually reappear in increasing number two or three days before the postponed paroxysm becomes manifest.

For curative effect, it is best to repeat the injection on each paroxysm day for 3 or 4 doses, after which oral administration may be substituted, and is to be kept up *for a sufficient period*, as already detailed.

Should the quantities and frequency mentioned not have the desired effect, it goes without saying that they are to be increased.

Such an increased dosage may be necessary from the first in *quartan* or *estivoautumnal* cases, in which 2 Gm. (30 grains) or more by mouth, or 1.5 Gm. (25 grains) by injection, may be needed daily, or at least on the paroxysm days.

In *pernicious malaria*, 1 Gm. (15.5 grains) or more of an appropriate

salt (*e.g.*, the dihydrochloride) should be given intramuscularly, or, better, *intravenously*, and repeated every two to four hours, more or less, for effect.

In *chronic*, *latent*, and *masked malaria* the attempt should be made, if possible, to provoke some frank manifestation of periodic character, according to the method of Archibald Billings, who early in the nineteenth century was accustomed, in doubtful cases of ague, to administer doses of Peruvian bark not sufficient to cure, but merely to reawaken the symptoms. The senior writer has modified this to correspond with our improved therapeutic and diagnostic facilities. An injection of 5 to 10 grains (0.3 to 0.6 Gm.) of quinine and urea hydrochloride is given and the peripheral blood examined for organisms. If these are found, and their type and period can be determined, the subsequent injections are timed, and the dose increased, accordingly. Otherwise full doses are given by mouth or by injection, at convenient times, singly or in divided portions, according to symptoms and result. In *brow ague* (malarial headache) and other forms of *neuralgia*, the neutral **quinine hydrobromide** is to be preferred, and may be given in wafer or capsule **with** a sufficient quantity of **ergot** to prevent tinnitus. Thus, 5 to 8 grains (0.3 to 0.5 Gm.) of quinine hydrobromide, with 3 to 5 grains (0.2 to 0.3 Gm.) of ergotin, may be taken before breakfast daily. If this dose does not prove efficacious, a like capsule may be given at night, or the daily dose of 0.6 to 1.3 Gm. (10 to 20 grains) may be divided into 3 or 4 portions. In cases showing considerable anemia, **arsenic** should be added in appropriate form and dose. Arsenic is often useful,

too, when there is no special anemia. **Strychnine** sometimes has a wonderful effect, and the association of quinine, strychnine, and arsenic is both rational and helpful. When there is *splenic* or *glandular enlargement*, **Lugol's solution**, or other form of **iodine** should be given. Iodine inunctions, with **iothion oil** (10 to 25 per cent.) or **vasogeniodine** (iodine petrox), 10 per cent. are useful. For great hypertrophy of the spleen (and liver) **ergot** may sometimes be added with benefit. In the *myalgic type* of chronic malaria, **salicylic salts**, especially **cinchonidine salicylate**, find applicability.

Contraindications.—The appearance of hemoglobin in the urine is said by some to be a toxic effect of quinine, and to indicate discontinuance of the drug. The writers have made no personal observations that will throw light on this subject. They have never seen hemoglobinuria (discernible to the eye) in cases of malaria (or, indeed, in any other infection) in which quinine has been given—even in the enormous doses they sometimes employ in acute lobar pneumonia, *e.g.*, 5 to 8 Gm. (75 to 125 grains) in twenty-four hours.

It is well known, however, that certain persons exhibit a peculiar susceptibility (so-called "idiosyncrasy") to the toxic influence of quinine. This is sometimes—but not commonly—manifested toward very small doses. Thus in a case observed by the senior writer, a child of about 6 or 7 years, who had some years earlier recovered from scarlet fever, had an attack of fever and delirium with general erythema, lasting about four hours, following a dose of 3 or 5 grains of cinchonidine salicylate. Subsequent observations showed no idiosyncrasy against other salicylic

compounds, but complete intolerance of cinchona derivatives. As in most cases of drug intolerance—and especially of quinine intolerance—the patient shows the signs of that condition which the senior writer has termed *autonomic* (or *vasomotor*) *ataxia*, and his family history is replete with instances of hay fever, migraine, hives, asthma, Graves's syndrome, visceral and vascular crises, and other autonomic and vasomotor disorders. When such an idiosyncrasy is known to exist, the administration of quinine must be carefully considered, but the question is not necessarily to be decided in the negative. The quinine reaction in the given case may be relatively unimportant; the risk of producing an eruption, itching, slight gastro-enteric disturbance, or even circulatory or nervous symptoms of mild degree, need not deter the physician from using the only certain means of cure in a serious infection. It is to be borne in mind, moreover, that only in exceptional instances is quinine intolerance absolute. Ordinarily a certain dose, perhaps as much as 5 grains or more, can be supported with little or no disturbance. Further, it is only *the excess over the parasitocidal quantity* that produces constitutional reaction. In such cases, therefore, it is possible to avoid a severe toxic reaction by carefully choosing the time and method of administration and dose to be administered. A single dose, slightly below the average effective quantity, and at the time of election, is best, *e.g.*, if by mouth, in an ordinary tertian case, 1 Gm. (15 grains) four hours before the expected paroxysm; if by injection under the skin or into the muscle, 0.6 Gm. (10 grains) two hours before the expected paroxysm, or even during the chill.

When, however, the susceptibility is so extreme as to constitute a veritable contraindication, some succedaneum to quinine must be sought.

Sensitiveness may be tested through the local reactions induced by applications of 1:1000 up to 1:10 quinine solutions to the scarified skin. In persons hypersensitive to quinine, cinchonine or cinchonidine may sometimes be given without difficulty. Some cases may be desensitized, according to O'Malley and Richey, by giving 0.005 Gm. ($\frac{1}{42}$ grain) of quinine bisulphate by mouth with 0.5 Gm. ($7\frac{1}{2}$ grains) of sodium bicarbonate, and $1\frac{1}{2}$ hours later, 0.1 Gm. (1 $\frac{1}{2}$ grains) of quinine bisulphate with 0.5 Gm. of sodium bicarbonate. This procedure is repeated daily, the second dose of quinine being, however, increased by 0.1 Gm. each day.—Ed.

Succedanea and Auxiliaries to Quinine.—Not only in cases of quinine intolerance, but also in certain cases in which the cinchona derivatives are well borne, but ineffective, other agents must be employed, either in place of the specific remedy or in supplement thereto.

Methylthionine chloride, better known as "medicinal methylene blue," has given good results in a number of cases, but is not always to be depended upon. It is best given in capsule, in doses of about 5 grains (0.3 Gm.) each, twelve, eight, and four hours, respectively, before the anticipated paroxysm. The patient must, of course, be advised of the discoloration of the urine and saliva that will ensue. If the drug is not well tolerated by the stomach, a **digestive ferment** may be added to the capsule, and perhaps a small dose of **opium**.

Where malaria proves refractory to quinine, **iodine** internally is effective. It does not kill the parasites but seems to ward off the febrile attacks and reactivate the quinine. The writer gives from 5 to 10 drops of a 10 per

cent. tincture of iodine twice daily. Roubachkine (*Presse méd.*, May 5, 1923).

Treatment of chronic malaria by a single intravenous injection of 0.003 Gm. ($\frac{1}{22}$ grain) of **mercurochrome** per kilo. (2.2 lbs.) of body weight in a 1 per cent. solution yielded a cure in all of the writers' cases. A reaction nearly always follows in 20 minutes to 3 or 4 hours, with general flushing, headache, rise of temperature of 1 or 2° C., chilly sensations or an actual chill, and usually vomiting, lasting 20 minutes to several hours. The reaction may be reduced by giving atropine and morphine in advance. The blood becomes negative for malaria within a few hours, and no patient had had a return of symptoms. Avison and Koo (*China Med. Jour.*, May, 1925).

Warburg's tincture has in the hands of the senior writer almost vindicated its early reputation. The action is severe and unpleasant, but the effect is beyond question. It must be used, however, according to Warburg's method, the induction of adequate perspiration being essential. It is indicated in cases of mild intolerance to quinine and in cases in which the ordinary use of quinine has been insufficient to produce complete recovery. Frequently in chronic and masked cases it is the promptest and most effective remedy at command, although it may to some extent be superseded by **arsphenamin**.

Warburg's tincture is a complex mixture frankly open to the reproach of polypharmacy, since it contains no less than 13 ingredients. Its inventor, Dr. Warburg, held its composition as a secret for a time, but finally made it public. Many modifications have been proposed, and some preparations now sold as Warburg's tincture probably contain few,

if any, of the original components. Indeed, some of these are not now readily obtainable. The tincture ought to be made as nearly as possible according to the following formula:—

℞ *Aqueous extract of aloes* .. 28 grains.
Rhubarb,
Angelica seedof each 448 grains.
Elecampane,
Saffron,
Fennelof each 224 grains.
Gentian,
Zedoary root,
Cubeb,
Myrrh,
White agaric,
Camphor,
Quinine sulphate ..of each 112 grains.
Dilute alcohol, enough to
 make 8 pints.

[The coarse vegetable portions of this list are to be ground into a coarse powder, and the myrrh and camphor, previously pulverized, added to them. The entire mass, less the quinine, is then digested for twelve hours in a well-covered vessel on a water-bath, the alcohol being prevented from evaporating as much as possible. The liquid is finally strained under pressure and the quinine sulphate added and dissolved.]

The patient must fast for at least six hours before treatment is begun, and take no food until the effect (free sweating) has been induced. After free purgation, $\frac{1}{2}$ fluidounce (15 c.c.) of the tincture is given undiluted, all drink being withheld, and at the end of three hours a second $\frac{1}{2}$ fluidounce is similarly given. Soon after the second dose, a violent aromatic perspiration comes on, and the fever is usually broken. The perspiration is encouraged by keeping the patient wrapped in blankets, with external application of heat, if necessary. Sips of cold water may be taken during the pack. Warburg's tincture is more effective in chronic

and relapsing cases than in the early and frank attacks.

Arsphenamin has come into use in the treatment of severe and obstinate malaria, both in acute and chronic forms, and excellent results are attributed to it.

Arsphenamin with **quinine** is much more effectual than the latter alone in malaria. The writers give an intramuscular injection of 1.2 Gm. (19 grains) of quinine at the beginning or during the attack, followed within 24 hours—preferably 6 to 12—by an intravenous injection of 0.15 Gm. of **arsphenamin**. This is repeated every week in mild tertian, increasing the dose of the **arsphenamin** to 0.3 Gm. In malignant tertian, they give 2 injections of quinine daily until the temperature is normal. Then 0.15 Gm. of **arsphenamin** is injected, and after this 2 Gm. (30 grains) of quinine by the mouth until the temperature has been normal for 2 days. The 2 drugs are then kept up once a week for 2 months and, during a third month, once a fortnight. **Iron** and **adrenalin** are useful adjuvants. Paisseau and Hutinel (Paris méd., Mar. 15, 1919).

Patients who could not take quinine found their symptoms subside after a single injection of **neoarsphenamin**, the parasites disappearing from the blood. Nieuwenhuyse (Ned. Tid. v. Gen., June 18, 1921).

In 8000 cases, the mortality was reduced to 0.2 per cent. in ordinary cases, and 6 per cent. in the malignant types, by means of **arsphenamin**. It was also found that **neoarsphenamin** in concentrated solutions, 0.9 Gm. to 2 c.c., acted as did higher dilutions, when given intravenously and by rectum. Nuñez (Amer. Jour. of Trop. Med., July, 1923).

In early cases of simple tertian malaria, an injection of **neoarsphenamin** is curative. In latent malignant tertian malaria, it has a provocative action. Pijper and E. D. Russell (South Afr. Med. Rec., May 9, 1925).

X-ray treatment of the spleen has been advised in chronic cases. According to Skinner and Carson, it relieves splenic pain, reduces recent engorgement of the organ, and may even cure cases resistant to quinine.

The writer endorses a daily dose of 2 or 3 mgm. ($\frac{1}{32}$ or $\frac{1}{20}$ grain) of **strychnine**, and approves of mild **X-ray treatment of the spleen**, which seems to exert a marked stimulating action. Silvestri (Rif. med., Oct. 2, 1920).

The Italian Government appointed a commission to ascertain the value of the **X-ray** in malaria. The author, its reporter, states that the X-ray is contraindicated in acute malaria; large doses may even promote a severe attack. Chronic enlargements of the spleen frequently subside, however, under X-ray treatment. Some forms of malaria with infrequent attacks are also cured. Busi (Policlin., Jan. 8, 1923).

Splenectomy has been advocated by a few observers. Kopylow removed the enlarged spleen in 13 cases, and found records of 187 other splenectomies in the literature. The general mortality was 25 per cent., and 3 of Kopylow's patients succumbed to lesions which could not be arrested by the operation. The remaining cases were found well 6 to 12 months after splenectomy.

Treatment of Pernicious Malaria.—The treatment of pernicious malaria consists in the energetic administration of **quinine**, preferably by intramuscular or, better, intravenous injection. From 10 to 25 grains (0.6 to 1.6 Gm.) of one of the soluble salts should be given without delay, and repeated at any subsequent paroxysm or, if indicated by the severity of the case, within two to four hours, and after that as necessary. When no further paroxysm develops, intramuscular injections should nevertheless be continued to the number of not less than 3 during the first week and 2 during the second.

Besides the use of quinine, prompt and effective symptomatic treatment is indicated, **morphine** being given to relieve discomfort and nausea, **stimulants** to overcome depression and weakness, **saline** purgatives to exert a derivative action in the comatose type, **opium** and **bismuth** to control diarrhea, **pituitrin**, **strychnine**, **cocaine**, **atropine**, **camphor**, or **musk** to sustain the heart and **cold sponging** or **external heat**, according to whether the temperature is febrile or subnormal, heat, of course, being employed invariably in algid cases and when collapse threatens.

Cathcart describes the treatment of collapse in malignant malaria as follows: In the milder cases a medium dose of **morphine** ($\frac{1}{4}$ grain—0.016 Gm.) hypodermically, with **hot-water bottles** and **blankets**, is indicated. This is combined with treatment of the predominating symptoms. In the dysenteric type a **starch** and **opium** **enema** should be given, with the buttocks well elevated. If vomiting is copious and persistent, **ice pills** are given, and all **nourishment by mouth** stopped for 12 hours. In either variety a full dose of **quinine dihydrochloride** (12 grains—0.6 Gm.) is given intramuscularly, and repeated each morning for 3 successive days. Weekly injections are, as a rule, sufficient after this. Where the peripheral circulation can no longer be trusted as a drug carrier, **venous infusion** of 2 to 3 pints (1000 to 1500 c.c.) of saline solution is performed, and the quinine solution added to the saline injection.

In a desperate pernicious case with cerebral symptoms the writer gave 15 grains (1 Gm.) of **quinine acid hydrobromide** on admission, 2 such doses in the next 24 hours, and five $7\frac{1}{2}$ grain doses in the course of the following 2 days, all intravenously. In 2 days all the parasites had disappeared. L. Rogers (Indian Med. Gaz., Nov., 1917).

In severe comatose cases in a malaria hospital on the Aegean Sea, the **serum of convalescents** in conjunc-

tion with quinine was found a life-saving measure. Seyfarth (Deut. Arch. f. klin. Med., Dec. 21, 1920).

In pernicious algid attacks the writer gives **caffeine** or **camphorated oil**, together with **quinine** intravenously, and **adrenalin**, 1 to 2 mgm. ($\frac{1}{65}$ to $\frac{1}{32}$ grain). Genevriev (Presse méd., May 20, 1922).

Intravenous use of **quinine acid hydrobromide** recommended for algid, comatose and cerebral malaria, or when the patient cannot tolerate cinchona febrifuge or quinine sulphate by mouth. The dose is $7\frac{1}{2}$ to 10 grains (0.5 to 0.65 Gm.) freshly dissolved in 15 to 20 c.c. ($3\frac{3}{4}$ to 5 drams) of sterile saline solution. In the majority of critical cases, 1 or 2 such intravenous doses, given during the first 24 hours, will speedily bring comfort, with a normal or subnormal temperature. The injections should then be discontinued and the patient commence the full 31-day oral course of quinine. Intravenous quinine will not prevent relapses. Acton and Knowles (Indian Med. Gaz., Apr., 1924).

MALARIAL CACHEXIA.

DEFINITION AND SYMPTOMS. — Repeated attacks of malarial fever—especially of the estivo-autumnal type and when inadequately treated—or a continuing and neglected infection, whether or not it has been attended by evident relapses, will give rise to a cachectic condition marked by feebleness, indisposition to exertion, loss of appetite, occasional blood-losses, gastroenteric disturbance, and obvious anemia. Nervous symptoms may be marked. The circulation may be extremely depressed; not rarely the heart is dilated, the pulse weak, rapid, and irregular, and paroxysmal dyspnea frequent and severe. The spleen is enlarged, often hard to palpation, and sometimes of enormous size. The liver is likewise enlarged; and

there may be more or less intense jaundice. Usually the complexion is yellow and muddy, sometimes with a peculiar pallor, especially of the lips, ears, and tarsal conjunctivæ.

DIAGNOSIS.—In individuals suffering as described, especially when there is a history of fever of irregular type, recurrence, and duration, search for the malarial parasite should be made. This is peculiarly true in the tropics. The complexion, unlike that of any other condition; the presence of free pigment or of pigmented leucocytes; an increase in the mononuclear percentage; perhaps a leucopenia, and the characteristic pallor and appearance of the red cells, will help in making the diagnosis, even when the parasite is not found in the peripheral blood. Sometimes if a small dose of quinine be administered, not sufficient to kill the parasites, they will be driven out of the spleen and bone-marrow (and possibly other resting places) into the peripheral circulation in sufficient numbers for demonstration. A fair dose of strychnine may have a like result. Splenic puncture is to be undertaken as a last resort, and only in cases of absolute necessity. The anemia and other symptoms may likewise be the result of an infection that has come to an end, and if even splenic puncture fails to reveal organisms, that possibility is to be considered.

The discrimination between malarial cachexia and kala-azar may depend upon success or failure in discovering Leishmann-Donovan bodies. Quinine, it is believed, has little effect on kala-azar.

PATHOLOGY.—The pathology of malarial cachexia has been cleared up since Banti's disease and kala-

azar have been clearly discriminated from it. The principal changes are in the blood, liver, spleen, and bone-marrow.

The pathological findings in the *blood* usually correspond to the degree of anemia. Dionisi and Big-nami describe four types of post-malarial anemia:—

1. Cases in which the blood shows alterations similar to those observed in secondary anemia, from which they differ only in that the leucocytes are diminished in number. In these cases recovery is the rule; a few, without further change in the blood-picture, terminate fatally.

2. Cases in which the blood shows alterations similar to those seen in pernicious anemia—especially the presence of megaloblasts. These cases end fatally.

3. Cases which are progressive, as the result of compensation by the marrow for losses brought about by the infection. At autopsy, the marrow of the long bones is found to be wholly yellow, while the marrow of the flat bones is also poor in nucleated red cells.

4. Chronic anemia of the cachectic, which differs from the foregoing types clinically and anatomically in that the special symptoms of malarial cachexia dominate, while one observes *post mortem* a sort of sclerosis of the bone-marrow.

The pathologic findings in the *spleen*, *liver*, and *bone-marrow* correspond closely to the pictures presented in chronic malaria and in acute malaria tending toward chronicity. The extent and degree of the tissue changes depend largely upon the intensity and duration of the cachexia.

PROGNOSIS.—When patients are unable to leave the locality in which they have contracted the infection, the prognosis is grave, as any intercurrent disease, because of lowered resistance, finds them easy victims.

When a change of climate is possible, the prognosis, while good under suitable treatment, should always be guarded.

TREATMENT.—The drugs of chief utility are **arsenic, iron, and quinine.**

Quinine is to be administered according to the rule in chronic infections, when parasites can be demonstrated or reasonably inferred to be present.

Fowler's solution may be given in ascending doses, until the point of tolerance is attained.

Arsphenamin or some one of the allied drugs may be administered in small doses, repeated weekly or fortnightly.

Sodium cacodylate or **atoxyl** can be given hypodermically in the usual doses, with caution.

Iron may be given in the form of **Basham's mixture, the Blaud pill, or the tincture of ferric chloride.** A solution containing a mixture of **iron and arsenic citrates** with **sodium phosphate** or other solution suitable for hypodermic use, may be injected as in other forms of anemia.

The "**esanophele**" pill is recommended by German pediatricists. Its formula is as follows:—

℞ *Quinine dihydrochloride* gr. iss (0.1 Gm.).
Arsenic trioxide... gr. $\frac{1}{64}$ (0.001 Gm.).
Ferrous citrate ... gr. v (0.3 Gm.).
Extract of gentian. gr. iiss (0.15 Gm.).

Mix. For 1 pill or capsule.

The following liquid mixture is useful:—

℞ *Tincture of ferric chloride* ℥lxxx to f3ij.
Diluted phosphoric acid. f3ij to f3iij.
Strychnine sulphate gr. $\frac{1}{8}$ to $\frac{1}{4}$.
Solution of potassium arsenite ℥viii to ℥xl.
Essence of pepsin,
Syrup of bitter orange-peel of each f3ss.
Water, sufficient to make f3ij.

Mix. Dose for an adult, 2 teaspoonfuls in water three or four times daily.

Iodine in the form of **Lugol's solution** (1 to 10 minims after meals *t. i. d.*), **sajodin** (0.1 to 0.5 Gm. one to three times daily), **iothion** inunction, or **iodipin** injection is often useful for short periods, from time to time.

Warburg's tincture has been used extensively, as in the treatment of chronic malaria.

Other measures to be employed are **hygienic, dietetic, and prophylactic**, and are elsewhere sufficiently discussed.

In chronic resistant infections and malarial cachexia, the authors recommend, in addition to quinine, 3 or 4 weekly injections of 0.45 Gm. of **neoarsphenamin** or other allied drug. Pratt-Johnson, Gilchrist, and Hay-Michel (*Brit. Med. Jour.*, Jan. 15, 1921).

In prolonged quinine treatment the drug should be discontinued periodically and **arsenicals** substituted. In anemia with jaundice and hemorrhage, quinine treatment should be regulated according to corpuscular resistance. **Hemoglobin, horse serum, and bone marrow** may be used. Where there is little response to quinine, **methylene blue** should be added. **Protein therapy** may be used when it is necessary to stimulate blood formation by the bone marrow. Comessatti (*Morgagni*, Jan. 31, 1922).

BLACK-WATER FEVER.

DEFINITION.—Black-water fever, or hemoglobinuric fever, is a disease

probably malarial, or closely allied, in origin, characterized by the voiding of hemoglobin in the urine. It occurs principally in the tropics. (See also HEMOGLOBINURIA, Vol. V.)

DISTRIBUTION.—Comparison of the countries from which black-water fever has been reported with the geographic data concerning malaria shows that the hemoglobinuric malarial and severe malaria co-exist in the same localities. It is best known in Africa, where it has been carefully studied, chiefly by British physicians. In India its occurrence is somewhat less frequent. Comparatively few cases have been reported from our Southern States, the West Indies, Europe, (Italy and Greece), and Asia Minor. The data are still too meager for exact statement. Europeans seem to be the chief sufferers in all climates.

SYMPTOMS.—Prodromal symptoms usually occur. Loss of appetite, malaise, pain in the back and limbs, and severe mental depression may forerun the attack. The paroxysm sets in with a violent rigor, the temperature rising to 103° or 105° F., and the first water passed is black in color. Indeed this may be the only symptom. The attack is generally accompanied by severe and continuous vomiting of dark green bile—a symptom which should cause the gravest concern. Jaundice appears early and may become marked. The spleen and liver become enlarged, tender or painful. Tympanites and epigastric pain are severe in many cases, while uncontrollable hiccough adds to the patient's distress. Drowsiness develops, gradually passing into somnolence, coma, and death. The urine is ordinarily increased in amount (but sometimes markedly decreased, leading

to suppression in grave cases), and maintains its black color. When death is escaped, there is a rapid fall in temperature, accompanied by sweating and an abatement of the distressing symptoms. The urine is generally free from hemoglobin on the day following the attack, but maintains its high color.

Convalescence may be entered upon, or relapses occur, with rigors and hemoglobinuria, and death terminate the case. Thrombosis of the heart, according to Plehn, is the commonest cause of death.

The blood is usually yellow and thin when taken for smears. Microscopically, the red cells may show chromasia and basophilia, and these appearances, indeed, should be looked for in all cases of malarial fevers, as some authors assert that they show a tendency toward the hemolytic action of quinine. The count may fall as low as a million. Peculiarly, the surviving individual erythrocytes show very little sign of the destructive process.

The principal changes in the white blood cells have been noted. During the paroxysm, a leucocytosis is present, the polynuclears being markedly increased—80 to 90 per cent. Afterwards there is leucopenia, with a mononucleosis of from 10 to 20 per cent. Pigmented leucocytes can nearly always be discovered.

Hemoglobinuric fever occurs in association with each of the 3 recognized species of malarial parasites, but, in the writer's opinion, the only one causally concerned is *P. falciparum*. In mixed infections, the finding of *P. vivax* associated with hemoglobinuric fever does not mean that it caused the disease, but only that it acted as the excitant of the attack. The disease results only from repeated and intense infections with pernicious malaria. An altered chemical reaction of the red cells is re-

sponsible for the production of black-water fever by this parasite. There is a darker staining reaction with the Romanowsky stains, together with "malignant stippling." These altered corpuscles may be regarded as foreign bodies capable of producing a specific hemolytic amboceptor, and this hemolytic substance will act only on cells so altered. J. G. Thomson (Proc. Internat. Conf. on Health Probl. in Trop. Amer., 1924).

Parasites will usually be found if the examination be made prior to the hemoglobinuric attack. Afterward they may not be discovered during life, but are generally to be found in the spleen *post mortem*. During life, quinine causes them to disappear rapidly.

The urinary condition is that of hemoglobinuria, not hematuria, and the microscopic findings will correspond. The urobilin and bile contents are high.

ETIOLOGY.—The factors causative of black-water fever cannot be given with certainty. Three hypotheses are put forth, all having the support of eminent names: 1. That it is malarial in origin. 2. That it is due to the toxic action of quinine. 3. That it is a specific infection, distinct from malaria.

The theory that it is a disease *sui generis* will be first taken up.

In cattle there occurs a well-known malady caused by a piroplasm and characterized by bloody urine; and this suggests a like origin for black-water fever. All that can be said on this head is that competent observers have sought for, but have not yet found, in the blood of patients with black-water fever, a similar piroplasm. Nor does hemoglobinuria specifically characterize the cases of piroplasmic infection in man thus far reported.

As to the quinine theory, further knowledge of the exact action of quinine in the blood is necessary before positive conclusions can be drawn. That it is hemolytic to a certain extent may be admitted, and that certain individuals show but slight resistance to its toxic action is well known. On the other hand, the drug is taken daily by thousands of malarial and other sufferers who do not pass black water. That quinine has apparently precipitated the attack of hemoglobinuria has been repeatedly observed. In fact, patients themselves will give the history of bloody urine first appearing after large doses of quinine. But this may possibly be owing to the great destruction of red blood-cells going on within the body, independently of the drug. During the actual hemoglobinuric crisis, Marchoux has found that quinine is not eliminated, but the drug reappears following the cessation of the symptom. Poch reports a case in which the red cells were diminished by 340,000, while no hemoglobin was found in the urine. These two observations tend somewhat to support the supposition that quinine is retained in the blood and exerts an actual toxic action upon the red blood-cells; but further investigation is required to determine the subject definitely.

The theory of malarial origin has in its favor the weight of tradition and many indisputable facts:—

1. No case of black-water fever is on record in which the hemoglobinuric crisis has not either supervened upon a malarial infection, or appeared in a subject who had previously suffered from repeated malarial attacks.

2. As a rule, it is the older residents in malarial districts who have had many, though slight, infections, that are the principal sufferers.

3. Black-water fever has a mortality 20 to 60 times as great as that of ordinary malaria, whence it would appear to be due to a highly virulent type of infection.

4. Statistics show that hygienic and medicinal prophylaxis reduces the liability to black-water fever.

5. Various observers, working independently and in different localities, report the finding of the malarial parasite in the blood in about 95 per cent. of cases before the attack; in 61 per cent. of cases on the day of the hemoglobinuric paroxysm; and in 17 per cent. of cases on the day following.

6. The presence of pigmented leucocytes of the mononuclear type and their increase in numbers, admittedly evidence of a malarial infection past or present, have been demonstrated in about 93 per cent. of cases observed by Christopher and J. W. W. Stevens, in Africa, and the malarial parasites were found in about 12 per cent. of their cases.

These facts prove that malaria is an important etiologic factor in black-water fever; but one must admit that it may possibly be a predisposing factor only—albeit a predisposing factor of the greatest weight. For the present, the writers incline to look upon black-water fever as a form of malaria, perhaps occurring only in persons having a special liability or in those whose quinine tolerance has been originally poor or diminished by disease—a double line of observation upon which data are wanting.

Bass has observed that calcium

salts when added in amounts but slightly in excess of the normal calcium content of the blood to cultures of estivoautumnal parasites *in vitro*, cause hemolysis of infected red cells, and possibly also of many non-infected cells. These salts do not affect normal blood similarly and the opinion is expressed that malarial hemoglobinuria is possibly to be explained through some such phenomenon.

PATHOLOGY.—Melanin is usually found in the spleen, liver and bone-marrow, and is of frequent occurrence in the kidney and brain. Hemosiderin can be found in the spleen. Pigmented leucocytes, macrophages, and malarial parasites may or may not be found. Degenerative changes may occur in all the organs; and the pictures, if at all typical, are essentially like those of acute or chronic malaria, previously described—a fact to be expected since the subjects of the disease are chiefly those who have had repeated infections.

DIAGNOSIS.—The typical attack is so characteristic that the diagnosis presents little difficulty to experienced observers.

The history, blood findings, and a careful physical examination will enable one to distinguish black-water fever from yellow fever, which is usually the main stumbling block.

PROGNOSIS.—Mild attacks have a good prognosis. When convalescence has occurred, prophylaxis and change of climate have much to do with the final outcome. The mortality is from 10 to 20 per cent.

TREATMENT.—The result of the experience of observers of black-water fever warrants the advice to

avoid quinine: first, because of its possible etiologic significance, and second, because, as a rule, the parasites rapidly disappear without it. Various authors, however, await the cessation of the hemoglobinuria, then administer quinine, some even in large doses.

If parasites should persist with a continuance of the fever, then the question of **quinine** administration becomes one of good judgment in the individual case. It may be commenced cautiously, a few grains at a time, and increased if the patient shows tolerance.

Immediate withdrawal of quinine advocated. The parasites disappear promptly with the attack. In the rare cases in which they do not disappear as readily, the writer gives **quinine** hypodermically—not by mouth, since vomiting is one of the most pronounced symptoms. The patient should receive plenty of **fluids**, and a blanket should be kept over him to promote perspiration. In 80 cases thus treated the death rate was 10 per cent. R. C. Connor (Proc. Conf. on Health Probl. in Trop. Amer., 1924).

Addition of serum from black-water fever patients caused hemolysis of erythrocytes from malaria cases in quinine solutions. Latent malaria may thus be revealed by means of a known hemolytic serum; likewise, a subject may be tested for susceptibility to black-water fever. When a previously positive reaction becomes negative, **quinine** may be resumed. Ghiron (Policlin., Jan. 1, 1926).

Possibly **arsphenamin** may be of service. **Warburg's tincture** has been advised; also **methylene blue**.

The general treatment is most important. **Rest**, of course, must be absolute. Free **elimination** should be obtained and it is possible that **hypodermoclysis** or even **endophleboclysis** with a slightly **hyperisotonic alkaline-**

saline solution might prove useful. **Champagne** is recommended when vomiting is excessive. **Nutrient enemata** are serviceable. **Ice** allays thirst.

Hearsey's treatment has been claimed successful, and is as follows: As soon as possible after the onset, **calomel**, with $\frac{1}{4}$ grain (0.016 Gm.) of **morphine** hypodermically to allay restlessness and vomiting, is given, the patient is wrapped in blankets, and **hot-water bottles** are put in the bed. An hourly dose of a mixture containing **liq. hydrarg. perchlor.**, mxxx (1.8 c.c.), and **sodium bicarb.**, gr. x (0.6 Gm.) to a tablespoonful of water, is given for the first 24 hours, and every 2 hours subsequently, until the urine clears. No food is given for the first 24 hours unless there is an inclination for it and absence of vomiting.

Good results from 2 intravenous injections daily of **caffeine sodio-benzoate**, morning and afternoon. Patients admitted almost moribund quickly react to its administration. Large amounts of **saline solution**, by hypodermoclysis or intravenously, are also given. **Quinine** is given to those cases in which malarial parasites are found. A. A. Facio (Proc. Internat. Conf. on Health Probl. in Trop. Amer., 1924).

Opium or **morphine** may be used with caution. **External heat** is useful and **nitroglycerin** may be employed tentatively to dilate peripheral vessels. **Strychnine**, **camphor**, **atropine**, and **musk** may be useful in combating a tendency to collapse. Possibly **pituitary** or **thyroid** preparations might be of service.

Various clinicians recommend other procedures, but **general treatment**, combined with **good nursing** and the **combating of symptoms** as they arise, often suffice for successful management of the case.

SOLOMON SOLIS-COHEN

AND

LEON SOLIS-COHEN,

Philadelphia.

MALE FERN. See **ASPIDIUM**.

MALT.—Malt (maltum, U. S. P.) is prepared from the seed of barley (*Hordeum vulgare*, order Gramineæ) by soaking them in water until soft. The water is then drained off and the grain is then placed in heaps in a darkened room; heat is spontaneously generated, and, by occasional turning, is prevented from rising too high. Under these conditions germination takes place. It is allowed to germinate until the plumule has grown to be half as long as the seed. The germination is then checked by the application of heat, which is maintained until it is perfectly dry. If the last heat be a low one pale or amber malt results; if dark malt is desired the heat applied is higher and the malt may be almost roasted. The former varieties are used in medicine; the latter yield porter and dark beers.

PREPARATIONS AND DOSE.—

Maltum, U. S. P. (malt), consists of yellowish to brown grains with a characteristic odor and sweet taste.

Extractum malti, U. S. P. (extract of malt), is made by infusing malt with water at 60° C., concentrating the expressed liquid at not over 60° C., and adding 10 per cent. by weight of glycerin. The product, a sweet, viscous, light brown liquid extract with an agreeable, characteristic odor, contains dextrin, maltose, a little glucose, and an amylolytic enzyme. It is capable of converting not less than 5 times its weight of starch into water-soluble sugars. It is soluble in cold but more readily in warm water. Its specific gravity is not less than 1.35 nor more than 1.43 at 25° C. Dose, ½ ounce (15 Gm.).

If, in making malt extract, the water is entirely extracted in a vacuum apparatus, a dry extract is obtained, which is the form used in the preparation of foods for invalids and children.

Another form of liquid malt (the so-called "diastasic extract of malt") is prepared by macerating well-malted barley in warm water for several hours; the infusion is then simmered with fresh hops at a temperature under 160° F., to retain the diastase and other proteins unimpaired, and then subjected to fermentation. The resultant liquid contains alcohol from a trace up to 10 per cent. It

resembles porter or brown stout in taste and appearance. The proprietary malt extracts are for the most part of this type, and actually possess little or no diastasic power.

PHYSIOLOGICAL ACTION.—Malt extract prepared at a sufficiently low temperature contains diastase, a ferment which in neutral or slightly alkaline media is capable of digesting starches. That such an action can be developed in the human gastrointestinal tract, however, seems unlikely, since it has been shown that even Takamine's diastase ceases to act in the gastric juice as soon as the acidity exceeds 0.1 per cent. It might, perhaps, digest some little starch in the mouth and stomach before its destruction by the hydrochloric acid. On the whole, malt preparations appear to be of but limited utility as starch digestants, and should be considered chiefly from the mere standpoint of nutritive value.

THERAPEUTICS.—Malt is a food element, since it contains all the nutritive substances of malted barley, which is rich in carbohydrates. It is possessed of a sweet, pleasant taste and can be taken alone, on bread, or in milk. It may also be taken in the form of an emulsion with an equal quantity of codliver oil. It may serve as a vehicle for iron, quinine, the hypophosphites, cascara, peptones, etc. It is useful in the wasting diseases, especially in *marasmus* and *tuberculosis*. Extract of malt is often retained when codliver oil is not tolerated. S.

MALTA, MEDITERRANEAN, OR UNDULANT FEVER (Neapolitan or Rock Fever of Gibraltar).—

This fever, called by various names, is a fever which is endemic in the Island of Malta, of common occurrence along the shores of the Mediterranean and in many parts of the tropics (India, Africa), and is more rarely met with in other parts of the world, cases having been reported in France, England, and even in the United States. (Endemic centers exist in goat-raising districts along the Rio Grande.) It is characterized by an irregular course, undulatory pyrexial relapses, profuse sweats, rheumatic pains, arthritis, and an enlarged spleen. The incubation period varies from six days to several months.

SYMPTOMS.—The symptoms are usually pronounced, though not especially characteristic.

There is a febrile attack with periods, somewhat variable in length, of normal temperature. The fever, while usually remittent, may be intermittent in character; as an exception it may be continuously high or low, and may change its type at any stage of the disease. The course of the disease also varies. It may be acute from the onset (malignant form), ushered in with chills and a rise of temperature to 104° or 106.5° F. (40° or 41.5° C.), associated with severe headache, lumbar pain, and general malaise. The pulse and respiration are increased, the latter more markedly. Diarrhea may first appear, to be followed later by constipation.

The subacute variety (intermittent form), the more usual, has a slower onset and more gradual development. It is in this form that rheumatic pains are most often present. In a few days the evening temperature rises to from 102° to 106.5° F. (39° to 41.5° C.), with remissions in the morning. Decline in temperature is marked by profuse perspiration.

The first attack may last from one to five days, and after an absence of fever for from ten to fourteen days a relapse occurs, but it is of short duration.

In rare cases (ambulatory form) symptoms are absent and the disease is only indicated by the presence of the infecting organism in the urine and of agglutinins in the blood.

DIAGNOSIS.—The presence of *Micrococcus melitensis* in the urine or blood, the complement-fixation test of the blood-serum, the agglutination test of the blood, and the skin test are the means of establishing the diagnosis.

Consideration should be given to (1) serodiagnosis, (2) blood cultures, and (3) the cutaneous reaction (Burnet). The first is based on the capacity of the serum to agglutinate *M. melitensis* in dilutions of 1:100 to 1:1000. Blood cultures, first carried out by Lemaire, serve to diagnose Malta fever on the 2d day. They can be used in the different forms caused by *M. melitensis* and *M. parameleitensis*: A sample of the blood is placed in serum (flask of 100

to 200 c.c. ordinary serum) at a temperature of 37° C. for 6 or 7 days; then ordinary agar or glycerin agar is inoculated, and on the 3d day, *M. melitensis* may be recognized. In the skin test, 6 hours after vaccination [intra-dermal injection of 0.1 c.c. of filtrate of a 20-day bouillon culture], a local edema is seen, with change in color and slight pain. There develops a round or oval plaque which is red, pale, or light gray, and 4 to 6 cm. in diameter. Nattan-Larrier (*Presse méd. hellénique*, July 1, 1924).

The blood-count is typical: the red cells are diminished; lymphocytes make up 50 per cent. of the whites; no eosinophilia.

ETIOLOGY.—The precise cause of Malta fever was discovered by Bruce in 1887 to be *Micrococcus melitensis*, which he obtained from the spleen pulp by cultivation, and which he established as the causal agent by the inoculation of monkeys, in which death occurred between the thirteenth and twentieth days. Clinical experience has shown that this fever depends directly on the use of goats' milk containing *Micrococcus melitensis*. Numerous cases, however, have developed in laboratory workers, in countries where the disease is prevalent, from handling cultures of the bacterium. Dargein and Plazy have reported a small epidemic traced to a pet dog. Transmission may occur through flies, by insect bites or by contact—urine or dust (Tappan).

PATHOLOGY.—The most marked post-mortem changes are found in the spleen, which becomes enlarged and soft, and is acutely congested, while the lymphoid cells in the Malpighian bodies are much increased.

There is present no hyperplasia of the lymphoid tissue of the intestines nor ulceration of Peyer's patches, as found in typhoid fever. There is, however, usually observed a congestion of the stomach, liver, and the intestines.

PROGNOSIS.—The prognosis is good, though the illness may be prolonged. The mortality is from 2 to 3 per cent.

TREATMENT.—The measures recommended include a liquid diet during the febrile period and hydrotherapy, either cold sponging or the cold bath or cold pack,

every third hour when the temperature rises above 103° F. (39.4° C.).

Autogenous vaccine gives the best curative results, though in the acute stage, according to Bassett-Smith, **antitoxic serum** should be given in addition.

Recovery obtained in 55 cases, mostly children, a single injection of **auto-genous vaccine** sufficing in many, others requiring 3 or 4 injections at 2 day intervals. De Finis (Pediatr., Jan. 1, 1923).

Methylene blue, given in cachets of $\frac{3}{4}$ grain (0.05 Gm.), two or three times daily, combined with milk-sugar, 4 grains (0.25 Gm.), when digestive disturbance is present, has been suggested.

Prompt cures from intravenous injections of 2 to 4 c.c. (32 to 64 minims) of 2 per cent. **collargol** solution. Ziemann (Deut. med. Woch., May 5, 1921).

Neoarsphenamin succeeds after failure of antiserums and vaccines, and may abort the Malta fever infection. De Partearroyo (Siglo méd., Jan. 19, 1924).

Stimulants may be necessary in severe cases to counteract cardiac and general depression.

The simplest means of prophylaxis consists in the **avoidance of goats' milk**. If it must be used, **pasteurization of infected milk** for twenty minutes at 145° F. (63° C.) will destroy the virus. Condensed or evaporated cows' milk may be used to replace the goats' milk. While the disease has no active effect on goats, its eradication is important. Vincent advocates active immunization of goats with *M. melitensis* and *paramelitensis* strains, each cubic centimeter of **vaccine** containing about 2000 millions of organisms. Nicolle and Conseille have found immunization in man feasible either by hypodermic injection or oral ingestion of vaccine. S.

MAMMARY GLAND AND LACTATION, DISORDERS OF.

ANOMALIES OF THE MAMMARY GLAND.—These consist of absence (**amastia**), incomplete development of (**micromazia**), and supernumerary (**polymastia**) glands.

Amastia.—Absence of both breasts is an extremely rare anomaly and is usually observed in women who are otherwise deformed, *i.e.*, monsters. The absence of one breast may be seen in a very few isolated cases. Greenhow reported a case of absence of the ovaries, with congenitally defective uterus, in which the mammae were absent, though there existed depressed rudimentary nipples and areolæ.

Micromazia.—Incomplete development of the mammae is rare, and is usually associated with some genital trouble.

This condition may be the result of faulty development from misfitting clothes, lack of proper physical exercise, etc., prior to puberty.

Polymastia.—Accessory breasts are found in probably 1 out of every 1500 to 2000 women, while the condition exists more frequently in men (Bruce and Lichtenstern), probably 1 in 500 to 1000. They rarely attain any considerable size and are rarely provided with nipples. They are usually located in the axilla or on the chest or abdomen. All of the glands may secrete milk during normal lactation in the female. Ahlfeld contends that the abnormality is the result of transference of mammary tissues in the early stage of development by means of the amniotic cells, which ordinarily go to form the breasts, but in this instance are distributed to the other parts of the body. Heredity no doubt plays an important rôle in their production. The largest number of breasts observed in any one person, to date, is 10.

Polymastia is hereditary in some families. An instance in which 4 generations had this anomaly is described. In 1

case both a miniature breast and a swelling without nipple and areola were observed in the same woman, in opposite axillæ. Tumors of the axilla, enlarging in pregnancy and keeping pace with the rapid enlargement and engorgement of the breast in the early puerperium, should be classed as polymastia. Apparently the masses without nipples have some connection with the normal breasts, possibly by an elongated duct, since they become smaller and less tense when the breast on the same side is drained by the infant. In 1 instance the swelling had been mistaken for an acute adenitis and incised, an opalescent white fluid exuding for 5 days. The patient should be assured that these accumulations of breast tissue have nothing in common with carcinoma of the breast. G. H. Klinkerfuss (Jour. Amer. Med. Assoc., Apr. 19, 1924).

Hypertrophy.—Non-pathological excessive development of the mammæ, while observed more frequently than the former conditions, is also of rare occurrence. There seems to be a predilection for young unmarried women, both breasts usually being implicated, and occasionally attaining immense proportions, necessitating amputation. In some of the indigenous negroes, the female breasts are naturally large and pendulous. Gould and Pyle recorded a case in which the breasts were sufficiently pendulous to be easily thrown over the shoulder during nursing. The anomaly is occasionally observed in the male sex. Moderate hypertrophy is not a contraindication to nursing. Lactation sometimes diminishes the hypertrophy. (See also PATHOLOGICAL HYPERTROPHY under TUMORS, this article.)

Two cases of enormous hypertrophy of the breasts in women of 23 and 27. The mammæ were of normal size until the age of 21 and

18, respectively. In the second case the breasts weighed separately 4.2 and 2.9 kg. after their removal. The enlargement seems to be merely an exaggeration of the physiological development of the breast. It may occur in the newly born, at the time of puberty or during a pregnancy, or without any connection with birth, puberty, or pregnancy, but 63.9 per cent. of the 72 cases found on record occurred in connection with puberty; 22.2 per cent. of the cases were connected with a pregnancy; 4 cases were in newly born infants. A. J. Juhle (Nordiskt med. Arkiv, xlv, Surg. Sect., No. 3, 1913).

In a young woman of 24, with enormous enlargement of the breasts, of 16 months' standing, 10 subcutaneous injections of 5 c.c. (80 minims) of human milk on alternate days were given. On the fifteenth day the breasts began to recede, and thereafter rapidly decreased in size until they resembled deflated balloons. Patel (Lyon méd., Apr. 27, 1920).

NIPPLES, ANOMALIES OF.

Congenital absence of the nipple rarely occurs, while acquired absence is usually the result of injury or supuration of the infantile breast.

Flat or depressed nipples (microthelia) may be congenital or acquired. The acquired form is ordinarily the result of corset pressure. By reason of this fact the condition has occurred more often than abnormalities of the gland proper. The so-called inverted, or decidedly depressed, nipple renders nursing impossible without the shield. If only moderately depressed, systematic massage, or careful development with the suction pump, during pregnancy will obviate much difficulty in nursing subsequently. No manipulation should be practised, however, during the period of the month corresponding with the regular

menstrual period, because of the tendency to produce abortion.

ULCERATION OF THE NIPPLE.

Erythema frequently occurs as a complication of lactation, particularly in primiparæ. Far more distressing, however, is a condition due to the fact that the colostrum causes maceration of the epithelium of the nipple; small vesicles appear, which, if not arrested by timely treatment, generally rupture. The *erosions* thus formed become covered with scabs, under which healing would normally occur; but sucking being continued, the erosions are transformed into ulcerating fissures, which sometimes involve quite deep destruction of tissue. Occasionally the small vesicles, instead of being discrete, become confluent, and, the entire epithelial covering of the nipple being compromised, a raspberry-like nipple results. These conditions are sometimes greatly aggravated by an unhealthy condition of the infant's mouth, which should always receive considerable attention, as cleansing with boric acid solution, before and after nursing and certainly when mammary disorders are present.

Fissures of the nipple are exceedingly painful, as already stated. They are most frequently met with at the apex and the base of the nipple, where it meets the areola. In the latter case the suction, made by the child in nursing, tends to tear them open; hence the excruciating suffering induced. They usually appear the fourth day, but sometimes earlier, and quite marked febrile symptoms may be induced.

TREATMENT.—It is evident that the prevention here, first, of the pri-

mary irritation and, if this is present, of the secondary manifestations, is indicated. Scrupulous cleanliness of the nipple will prevent accumulation of colostrum and the primary erosions; hence this should be insisted upon. Both nipples should be carefully washed with a weak **boric acid solution** not only after nursing, but immediately before, and they should be carefully dried.

When local lesions exist, **suspension of lactation on the affected side** and, instead, milking the breasts by gentle **palmar massage** cause them to disappear in a few days, provided adequate cleanliness is insured. When but one nipple is involved, therefore, it can be allowed to rest, the other being used for suckling. Buccal suction, by the nurse or the husband, was formerly recommended; but the condition of the mouth being unknown, emptying the breasts by palmar massage is preferable.

Simple *erosions* usually yield promptly to the daily applications of **compound tincture of benzoin** and the application of **bismuth subnitrate** and **castor-oil emulsion** after each nursing.

Eczema of the nipples is sometimes taken for simple erosions, but it yields to the same measures. The **salicylic acid ointment** is also of value.

When *fissures* are present, the same measures are indicated, but in addition stimulation by means of **nitrate of silver** is required. The nipple being washed and carefully dried, the mitigated stick, finely pointed, is gently applied to each fissure; the moisture within the latter affords precisely that needed to obtain the best effects from the remedy. Care should be taken not to touch the surface of the nipple.

When both nipples are affected, the infant should be given the breast as early as practicable, *i.e.*, as long as the mother can stand the pressure of the secretion. Prior to each nursing the nipple should be carefully washed and a **nipple-shield** employed to protect it. The infant sometimes shows evidence of ill humor and refuses to suck through them; but a little patience usually controls the situation. A glass shield with an India-rubber tip is to be preferred, providing caution be taken to avoid bruising the breast and establishing an areolar inflammation. It should be kept scrupulously clean and washed immediately before and after using. If the infant refuses to use the tip, wetting the latter with sweetened water generally acts as an inducement. The remedial measures already indicated are then resorted to.

In septic fissure a dressing of gauze soaked in 1:1000 **mercury bichloride** solution is useful. It must be kept damp, and very completely washed off before the baby feeds. The same applies to 1:80 **phenol**. Sometimes 1 or at most 2 **hot fomentations** on the nipple will improve the condition, after which **compound tincture of benzoin** may be painted into and over the crack. V. I. Russell (Lancet, Dec. 20, 1924)..

Twelve cases of slight fissures treated with the **ultra-violet rays**. The exposures, on alternate days, began with 2 minutes, gradually lengthened by 2 minutes up to 10 minutes. A single exposure sometimes relieved the pain. Complete recovery occurred in 1 to 2 weeks. Chatin (Bull. de l'Acad. de méd., July 21, 1925).

The other disorders to which the nipple are subject are so intimately connected with those of the mammary gland proper that they cannot be treated separately.

MASTITIS.

Three forms of inflammation of the mammary gland are recognized: the *subcutaneous*, the *parenchymatous*, and the *submammary*.

Subcutaneous Inflammation.—This is not frequently met with and, though it may present itself in various parts of the organ, it usually confines itself to the areola. It is always due to infection through the lymphatics. The gland proper is not involved. Its development is that of an ordinary pimple or boil. The spot first becomes red, warm, and extremely sensitive. When located in the areola, several small, boil-like projections usually present themselves, which ordinarily proceed to the stage of supuration. They sometimes assume an erysipelatous character.

Parenchymatous Mastitis.—An inflammation of the gland proper, terminating in resolution or abscess formation. There are two distinct forms: one beginning in the interstitial tissues, when the acini become involved; in the other the inflammation develops in the acini and the interstitial tissues become involved. It was formerly believed that impediment to the escape of milk, through obstruction at the nipple by stagnant milk, epithelium, etc., gave rise to this condition, but modern researches have shown that all forms of mammary abscess are of microbic origin. Microorganisms originating from the infant's mouth or from hands contaminated with lochial or decomposition products from the gland, that have accumulated on the clothing and become infectious, infect the nipple and readily reach the deeper parts directly or through the lymphatics.

The first sign is the presence of in-

duration of the tissues of the organ. At first no suffering is experienced, but pain is finally noticed while the infant is suckling. The presence of an inflamed area with heat, redness, and swelling now becomes manifest. The hard mass previously noticed becomes very sensitive and edematous, and the organ, as a whole, becomes heavy. Should the inflammation persist for more than thirty-six hours it has gone beyond the resolution stage and, if in the parenchyma proper, there will be a chill, with sharp temperature rise, rapid pulse, etc. If primarily in the interstitial tissues, there will occur rigors only. Rigors or a distinct chill indicate impending abscess formation. The skin over the abscess finally becomes purplish and less tense, and fluctuation is soon obtained. When several foci of inflammation are present, they may suppurate successively, and the series of abscesses thus developed may destroy the entire gland, and the sufferings of the patient continue months. Septicemia and gangrene sometimes complicate such cases. Even in the comparatively benign cases generally met with, the general symptoms are sometimes quite marked.

Abscesses are most frequently found in the following situations: (1) Sub-areolar abscess. This appears close to the nipple as a reddened area with fluctuation. Usually the rest of the breast is unaffected. (2) Abscess in a dilated duct, deep to the nipple. This is recognized by a markedly prominent and painful nipple surrounded by an inflammatory zone, in which deep edema is present, and possibly fluctuation. There may be a purulent discharge from the nipple. This type will extend outward into the parenchyma unless opened. (3) Parenchymatous abscess. The overlying

skin is red and edematous, and the breast feels irregularly hard. This is commonest in the lower half of the gland, but a decision must be made as to which lobes are involved and the treatment varied accordingly. (4) "Shirt-button abscess." This is recognized by marked prominence of the breast with but slight signs of inflammation in the gland itself. Fluctuation may be detected at the outer margin of the lower half of the gland. J. B. Hume (Lancet, Nov. 7, 1925).

Submammary Abscess.—The space between the gland proper and the pectoral muscle over which it lies is furnished with a pad-like layer of connective tissue. Occasionally this becomes the seat of an abscess, the result of extension of the inflammation from the gland proper,—encouraged oftentimes by the use of ice-bags, when used at any time except in the beginning. When the suppuration is extensive, the breast is raised and may be moved from side to side. The local symptoms differ entirely from those of the former condition. There is but little redness, but the tissues at the base of the organs are edematous and the neighboring glands are generally enlarged and painful to the touch. There is a deep-seated, dull pain, radiating to the arm and often increased by the motion of the latter. There is a chill and marked fever, especially when the pus has formed, and lasting until the latter is evacuated. Pus usually points not far from the axilla, and when the abscess opens of its own accord, which rarely happens, a fistula may ensue. It may point in the direction of the lacteal ducts, a puriform fluid then being secreted with the milk.

Mastitis in nursing women is almost always due to stasis, caused by insufficient evacuation of the

glands. The infection of the stagnant secretion is due to bacteria which under normal conditions vegetate in the lacteal ducts without giving rise to any mischief. If infection, as is commonly assumed, resulted from fissures we would more frequently observe cutaneous inflammations, phlegmons, or erysipelas of the integument of the breast. A. Schiller (Wiener klin. Woch., Nu. 26, 1911).

PATHOLOGY.—In parenchymatous inflammation, according to Blumm, the rapid proliferation of micro-organisms in the gland structures causes fermentation of the milk, and transformation of its sugar into lactic and butyric acids. The casein becoming coagulated, the glandular structures become engorged with the coagula, and inflammatory changes soon follow. The periglandular tissues become infiltrated with bacteria and leucocytes, while the epithelial cells lining the glandular structures swell, desquamate, and disappear. Purulent miliary foci soon form in great numbers, and adjacent foci unite. Irregular cavities are thus formed and crossed by shreds of partially destroyed tissues. In the walls of these cavities leucocytes accumulate, which stop the progress of the microbes, preventing further spreading of the process of disintegration.

TREATMENT.—The treatment of *subcutaneous inflammation* of the breasts in the early stages requires supportive measures and the application of a **boric acid-alcohol** solution or 25 per cent. **ichthyol**; in the event of abscess formation **incision** and **evacuation** of the pus, followed by **antiseptic dressing**, are indicated. It is not always necessary to remove the child from the breast in this form of **mastitis**.

The use of an ice-bag is a confession of inefficient prophylaxis. The prophylactic care of the breasts of nursing mothers is as follows. **Surgical cleanliness** daily carried out with as much care as for preparation for an operation on the breast. **Rest** for the nipple and for the breast as for other organs that must functionate though temporarily crippled. **Dry and moist heat** and **pressure**, properly utilized for their well-known hydro- and mechanico-therapeutic values. The means of utilizing these principles are the lead shield, hot-water bags or hot compresses, and the mammary binder. R. C. Norris (Amer. Jour. of Obstet., vol. lxxvii, 46, 1918).

The treatment of subcutaneous inflammation does not always vary from that indicated for the nipple. An important point in this connection is that any **incision** made should **radiate from the nipple**,—i.e., cutting away from the latter, toward the periphery of the breast, as the spokes of a wheel radiate from the hub. The milk-ducts are thus avoided, and a free incision can be made without danger, if it is necessary.

Solution of **rubber and benzin** with 1 per cent. **formalin** is useful as a protecting coat for the skin. The benzin evaporates, leaving a thin, impervious coating fitting tightly over the skin, while the formalin has direct bactericidal action. The writer first cleanses the parts with **iodine-benzin**, then paints them with tincture of **iodine**, and then applies the rubber mixture. This preparation before laparotomies and vaginal operations has been found successful in eliminating all tendency to wound infections. Applied to the nipple, it protects it against cracks and fissures, and thus tends to ward off mastitis. Döderlein (Centralbl. f. Gynäk., Bd. xxx, Nu. 49, 1907).

The writer found in a large number of superficial abscesses in various parts of the body that, by simple

puncture and evacuation of pus, followed by irrigation with a solution of **mercury bichloride** and subsequent injection of tincture of **iodine**, or of **Lugol's solution**, the abscesses healed with great rapidity and insignificant scarring; he adopted this plan of treatment in 6 cases of breast abscess, with encouraging results. S. Seff (Amer. Jour. of Surgery, July, 1911).

Acute puerperal mastitis is distinguished from actual abscess by the absence of an area of fluctuation or a central softening. Until abscess exists the treatment is similar to that of milk engorgement, *viz.*, the **breast** should be **supported** by a thick pad of cotton with a bandage passing beneath it and over the opposite shoulder. The **nipple** should be **cleansed** with pledgets soaked in boric lotion, and the **breast pump** employed. **Lotio plumbi** may give considerable relief. If the need for breast feeding has ceased a **belladonna plaster** should be used; **fluids** should be drastically **diminished**, and if the breast is not too painful it should be firmly **bandaged** over layers of cotton after evacuation with the breast pump.

In doubtful abscess, if constitutional symptoms are severe, an **exploratory incision** may be made. If pus is not found, congestion will be relieved and drainage provided in the pre-suppurative stage.

The incision should be lightly packed with gauze soaked in **flavine** or **acri-flavine**, or better, in an emulsion of equal parts of flavine and **liquid petrolatum**.

In actual abscess, in order that the whole breast shall not become infected and later fibrosed, the affected lobes should be thoroughly opened up under a general anesthetic. In subareolar abscess or abscess in a dilated duct deep to the nipple, the **incision** should start at the base of the nipple and extend radially over the center of the infected area to the outer limit of the zone of induration. The incision should be deepened until pus is found. The completely opened cavity is

mopped out and temporarily packed with gauze. Later inspection will show whether pus is welling up from a deeper abscess. J. B. Hume (Lancet, Nov. 7, 1925).

Bier's method applied to the treatment of mastitis in its various forms is of the highest value. It consists in applying, as soon as the initial symptoms of the lymphangitis make their appearance, a large cup over the inflamed gland for ten minutes three or four times daily. It gives constant success upon the condition that it is applied as soon as the infection makes itself evident, that is to say, when the lymphangitis or galactophoritis is in an early stage, before the glandular *culs-de-sac* or the surrounding tissues have become invaded. Under these circumstances the pain rapidly disappears, the tumefaction diminishes, and the glands retain intact their essential anatomical elements, with the result that nursing may be resumed very shortly.

Treatment by **Bier's passive hyperemia** recommended in puerperal mastitis. Among 42 women in whom this procedure was applied, recovery took place without incision in 23. For patients in whom incision of the abscess has already been necessary the measure likewise gives good results. Silzer and Meyer (Munch. med. Woch., Oct. 2, 1925).

Mesnard undertook a long series of experiments at the St. Antoine Hospital, and found that Bier's method gave favorable results as compared with other methods. Thanks to this treatment systematically applied for a period of over a year, only a single case of mammary abscess occurred in the lying-in department of the above-mentioned hospital.

In Pfannenstiel's clinic at Kiel during the last four years 44 patients

with acute mastitis were treated with Bier's cupping apparatus. Abscesses developed in 9 per cent.; this complication was probably due to defective technique, the suction being applied too vigorously. Nutritional disturbances are liable to be induced by overenergetic suction, with the formation of an abscess in consequence. **Bier's suction hyperemia** proved superior to all other methods of treating acute mastitis if correctly applied, but the slightest excess in intensity soon avenges itself. Jager (Deut. med. Woch., Apr. 8, 1909).

The writer has treated successfully 30 patients with **Bier's method**. Graham (Edinburgh Med. Jour., Nov., 1909).

Bier's stasis hyperemia gives a prompt cure in the early stages and prevents suppuration. If pus has formed, nursing should be continued on the healthy as well as the affected side if the abscess is so situated that the nipple need not be bandaged. Large incisions and drainage are preferable to punctures and hyperemia. As soon as possible after operation the child should be allowed to nurse on the affected side. As a rule, normal lactation is restored within a few weeks. Schiller (Wiener klin. Woch., Nu. 26, 1911).

At Basel the woman's breasts after the birth of a child are kept constantly covered day and night with a little pad of gauze moistened with a 4 per cent. boric acid solution. A piece of rubber tissue overlaps the pad and sticks to the skin, and a towel is then laid over both breasts. The pads are renewed each time after the infant nurses. By this simple means since 1904 the proportion of cases of puerperal mastitis has dropped from 6 to 0.9 per cent., and suppuration occurred in only 0.2 per cent. in 8528 parturients.

The mastitis is treated with 5 per cent. **phenol-glycerin** dressings and ice, **suspending the breast** to insure keeping it still, **drawing the milk with a breast-pump**, and **evacuating**

pus through a minute incision, introducing the finger or forceps to reach all the foci. Bier's method of suction hyperemia has not proven satisfactory. It spares the incision, but this is outbalanced by the liability to local erysipelas and other complications. Eicher (Beiträge z. Geburts-hülfe u. Gynäk., Bd. xvii, Nu. 2, 1912).

The writer recommends **frequent aspiration** and the use of **continuous pressure**. The principle of this is that the aspirations be repeated frequently enough to keep the pus cavity dry and that the continuous pressure be sufficient to prevent the blood current from showing in the mammary veins. The cases reported show that the abscesses so treated heal in from 4 to 9 days. I. Gardiner (Trans. Amer. Med. Assoc., June 12, 1919).

In **submammary abscess** the gland projects outward and seems to rest upon a pillow of fluid. The quantity of pus is sometimes very great,—over a pint,—the connective tissue yielding on all sides to form a large cavity or pocket. When the abscess does not point in any special direction, the presence of pus may be determined by means of an aspirator needle inserted at the base of the gland. An incision can then be made at the lower border of the gland, the incision always **radiating from the nipple**. If the breast is pierced, a better method is to make an incision at the lower border of the gland, lift it up, and **evacuate the pus** from beneath. The pus being finally evacuated with antiseptic precautions, the abscess should be washed out with a 2 per cent. solution of **carbolic acid** or **boric acid**, 2 parts, and **alcohol**, 1 part, and **drained with iodoform gauze**.

Analysis of 41 cases of cold retro-mammary abscess. Active surgical measures are here indicated. Puncture and modifying injections should not be considered, as the primary

lesion is retrocostal or pleural and practically inaccessible. The question whether to operate or not is merely the question of the patient's ability to withstand the operation. Hardouin and Marquis (*Revue de chir.*, July 10, 1908).

For incipient abscesses, the use of a *staphylococcus vaccine* is advocated, beginning with doses of 25 to 50 million bacteria and ascending gradually. The incipient abscesses may promptly retrogress without actual suppuration. In the more advanced cases, hard areas soften, the abscesses open spontaneously or with a very small incision, and the course is definitely shortened. Bodin (*Monat. f. Geburtsh. u. Gyn.*, Feb., 1922).

In *parenchymatous inflammation* the infant must be weaned; otherwise, the lesions will proceed from bad to worse. The breast must be immobilized with a snugly fitting **breast binder** or **adhesive straps**. **Ice-cold compresses** may be used in the very early stages, but not later, frequently renewed. The application of equal parts of a saturated solution of **boric acid** and **alcohol** is valuable. A weak solution of **bichloride of mercury** may be applied every three hours and kept moist with a covering of impermeable dressing. **Belladonna ointment** and **lead-water and laudanum** are recommended by various clinicians. **Saline cathartics** are useful as derivatives, provided the patient is not too weak. Fluidextract of **phytolacca decandra**, internally, is sometimes of value when the inflammation is inclined to be subacute or chronic.

When fluid collections suggesting abscess occur, **massage toward the nipple** will almost invariably free the duct, and **rest** of the breast for 24 hours effectively prevents the breaking of the capsule around the gland tissue and involvement of the fatty tissue. Where there is pain, a fluctuating mass

and high temperature, white absorbent cotton serves as an indicator; ordinary milk will not stain it, while the contents of the sac invariably shows a dirty greenish yellow. H. M. Little (*Med. Rec.*, Apr. 30, 1921).

In parenchymatous abscess in the lower half of the gland, an **incision** should be made starting just within the areola, extending radially over the fluctuating lobe, and ending at the periphery of the breast. It should be carried well into the lobe, the finger introduced, and any loculi in adjacent lobes containing pus sought for and opened. Care should be taken that a pus pocket in the region of the nipple is not left unopened. A $\frac{1}{2}$ inch drain of red rubber, with thin walls and several side openings, should be inserted, and the incision lightly packed with gauze soaked in **flavine and liquid petrolatum** emulsion. After packing daily for 2 days **Dakin's solution** should be substituted. Any débris or small sloughs are best removed by irrigation with saline solution. The packing should be gently laid in from end to end of the wound in long strips. H. B. Hume (*Lancet*, Nov. 7, 1925).

When the presence of **pus** is ascertained, it should be **evacuated** under strict antiseptic precautions, an **incision** $\frac{1}{2}$ inch in length, **radiating from the nipple**, being made in the most dependent portion of the organ. The **cavity** is then **washed out with an antiseptic solution**. When the abscesses are multiple or involve a large portion of the gland, **counterdrainage** is indicated, by means of **iodoform gauze** or **rubber tubing** or the **cigarette drain**.

Good results are obtained by treating an acute mammary abscess by **Mundé's sponge compression method**. A large, flat, coarse bathing sponge is hollowed to admit the breast, is freed from foreign matter, and treated with hot **phenol** solution. The abscess is opened over the seat of fluctuation by an **incision** radiat-

ing from the nipple, the **pus evacuated**, and the **abscess cavity washed out** with a mild **antiseptic or saline solution**. The sponge is then dipped in hot sterile or carbolized water and wrung out in a towel. It is then placed over the breast, the walls of the cavity being held in apposition; is covered with oiled silk, and is evenly and firmly compressed against the thorax with wide rubber bandages. This dressing is changed daily, and the sponge cleaned, but the abscess cavity not interfered with. Dear- den (Am. Jour. of Surg., Oct., 1912).

The writer has found Chaput's **filiform drainage** with thread, wire or a very fine bougie a great improvement over other methods. The thread is drawn entirely through the abscess, and drainage proceeds incessantly and effectually, the minute openings in sound tissue not filling up, as they are free from dead space, while they do not favor introduction of air, are painless and do not bleed. Di Sant' Agnese (Policlinico, July 15, 1917).

The general health requires considerable attention, the strength of the patient bearing considerably upon the recovery. Good food, tonics, and pure air are important adjuvants.

GALACTOCELE.

This condition is due to occlusion and distention or rupture of one or more lactiferous tubes. In the latter case the milk permeates the connective tissue of the gland.

SYMPTOMS.—Two varieties of this rather rare condition are met with: in the one the accumulation of milk, within the duct or the connective tissue, occurs near the nipple and superficially. The appearance is typical: more or less large, knob-like projections or swellings form at the apex of the gland. It usually appears suddenly while suckling the infant, when rupture of the tube occurs without causing much local distress. In

simple dilatation from occlusion, which may occur during pregnancy, although more frequently during lactation, the growth is gradual.

The second variety of galactocoele occurs in the substance of the organ, forming one or more irregular lobular projections, which are quite firm under pressure, especially in cases of long standing. In the latter, when due to rupture of the ducts, the accumulated secretion is often found hemmed in by a protective cyst-wall. When the duct is simply dilated, the wall is formed by the lactiferous tube itself; this form likewise appears more or less suddenly. In some cases the gland becomes very large, and as much as 5 quarts of serous, milk-like fluid have been withdrawn by means of the trocar. There should be no enlargement of the axillary glands.

TREATMENT.—Aspiration is sometimes sufficient to cure small cysts; but in the majority of cases, it is best to **open** the distention antiseptically and to **drain**.

BENIGN TUMORS.

Benign tumors of the breast include *hypertrophy*, *adenoma*, *fibroma*, *lipoma*, *myoma*, *calcification*, *osteoma*, *dermoid* and *hydatid cysts*, besides *galactocoele*, which has been described.

Every palpable mass in the breast of a woman should be regarded as malignant until proof is obtained of its benignity. Previous to the age of 25, lesions of the breast are, as a rule, benign. They include intracanalicular myxoma, fibroadenoma, and diffuse virginal hypertrophy. In women over 25 every tumor of the breast should be explored without delay. They may be malignant or doubtful. Bloodgood (Amer. Jour. Med. Sci., Feb., 1908).

Tumors of the breast, though rare in children, occur in both sexes and

at all ages. Benign tumors in the young are more common in mammary gland than the malignant, the most common varieties being fibro-epithelial growths and angiomas. Sarcomata are rare and carcinomata almost unknown before puberty. Girls are less often affected than boys, but the difference is not so great as in adults. Angiomas are usually congenital or appear in infancy; fibroadenomata develop as puberty is approached. The smaller benign tumors may cause no inconvenience, or they may give rise to pain, tenderness, and inconvenience on account of their size. Sarcomata show the symptoms usual with that form of tumor. Jopson, Speese, and White (*Annals of Surg.*, Nov., 1908).

HYPERTROPHY.—The condition referred to here is a pathological rather than an anomalous condition such as that referred to in the earlier part of this article. Its onset is quite insidious: the breasts begin to swell and steadily increase in size within a few months, until they have attained quite noticeable proportions. The enlargement may affect both organs, but sometimes only one of them, *i.e.*, when the process follows traumatism. The breast keeps the shape of a hemisphere, but it is much firmer than usual. When, however, it has become very large, its weight causes it to fall below the abdomen, sometimes down to the knees, the upper portion forming a more or less large cutaneous pedicle. It sometimes assumes very great dimensions. There is no tendency to spontaneous recovery in the virginal type, while in gravidity spontaneous recoveries have been observed.

The menstruation, as a rule, is disturbed. Pains appear, which, though rare at first, become more and more pronounced. The patient, how-

ever, complains especially of extreme fatigue caused by the enormous weight. In some cases the breasts acquire almost incredible proportions, one-third the body weight; the patient loses her appetite, and occasionally dies of weakness and prostration, the autopsy showing no other alteration than the enlargement. The chief part of the hypertrophy is due to an



Hypertrophy of the breasts during pregnancy.
(Wieshaupt.)

increase of the connective tissue. Microscopically the tissues resemble very closely adenofibroma.

Treatment.—Iodide of potassium used early and in large doses and moderate pressure exerted by means of a flannel or rubber bandage sometimes retard or arrest the growth. If the tumor continues to grow, complete excision is the only treatment. Lactation seems to cause diminution, and has been followed by a cure in a few instances. The oppo-

site may be the case, however, as in the patient shown in the illustration.

INTRACANALICULAR MYXOMA.—Closely allied to the above form, this variety of tumor is that most commonly met with in the young female, developing most frequently during puberty hypertrophy. The hypertrophy is limited to the intralobular stroma of the gland. It is subject to the same treatment.

In case of myxoma of the breast the tumor was so large and cumbersome that the patient, when sitting down, was obliged to rest it on a table or on the arm of a chair. The patient was only 38 years old and the tumor, which weighed 16½ pounds, was first noticed three years previously. It was entirely discrete and was removed easily. During the last two or three months the tumor had grown very rapidly, due to a sarcomatous metaplasia. Graves (*Boston Med. and Surg. Jour.*, Apr. 18, 1907).

ADENOFIBROMA.—Adenofibroma is frequently observed, and may appear at any age, but is usually met with between the ages of 15 and 45 years—during the sexual life. Menstrual disturbances and contusions of the breast are thought to exert a certain pathogenic influence.

Symptoms.—Adenofibroma grows insidiously; pain is only present in exceptional cases, and is usually increased during the menstrual period. The growth rolls under the fingers, and its surface is generally irregular, though the skin is unchanged and elastic under pressure. The nipple is not retracted, but there occasionally exudes from it a serosanguineous fluid.

The subcutaneous veins are only slightly, if at all, dilated, except when the tumor is very large. The axillary

glands are usually normal, and the patient's general health is good. Very rarely these growths have been known to attain a considerable size in a short time, and the distended skin to become thinned and ulcerated; but the cutaneous tissues remain free and loose, and the ulcerative process presents none of the characteristics of cancerous ulcerations.

Treatment.—The progress of small adenomata may be retarded by the local use of iodine and by slight compression, but, if they continue to increase in size, they should be excised. It is important to remember that the excision should be complete, the least remnant becoming a focus of recurrence.

Adenoma of the primary type or stage in persons under 30 years of age may be removed together with its capsule and a wide margin of the adjacent stroma and a very favorable prognosis given; but in women over 30 years of age, even this type may be potentially malignant. Cases of secondary hyperplasia should be considered as precancerous. Gillette (*Trans. Amer. Assoc. Obstet. and Gynec.*; Oct. 25, 1919).

LIPOMA.—Lipoma may exist in the breast in single or multiple form. A small lipoma would only be recognized by an exploratory incision, while a large growth should not be difficult to differentiate from an intracanalicular myxoma, which it most resembles.

CALCIFICATION.—Areas of calcification have been observed in the walls of simple cysts by Billroth, but are more frequently noted in conjunction with adenofibroma, scirrhus, carcinoma, and sarcoma.

CYSTS.—These growths are occasionally met with, and present as

symptom only a localized enlargement, with unmistakable fluctuation.

Cysts are usually due to dilatation of the glandular portion of the lacteal tubes, followed by obliteration of the excretory duct; occasionally the sac develops in the interstices of the gland. In the tubular form a clear or gelatinous serum is exuded; the parenchymatous cysts, however, usually contain a sanguineous fluid. The cystic walls form part of the surrounding tissues, and cannot be peeled off from them without lacerating the latter.

A peculiar type of cystic disease of the breast has been described by Reclus. It consists in the development in the healthy tissues, and in both breasts at once, of a large number of cysts, varying greatly in size from that of a pinhead to a hen's egg, and containing a more or less thick liquid, which may be either quite transparent or dark. Their growth is gradual and causes but little, if any, suffering. They feel like hard subcutaneous masses which cannot be said to fluctuate.

Latent manifestations of Reclus's disease (cystic epitheliofibrosis of the breast) were found in 25 per cent. of girls and women below 40 and in 33 per cent. of elderly women. Proliferation of the mammary epithelium to an extent that would be regarded as suspicious in other organs results from the fact that this epithelium is easy to irritate. Removal of the tumor is called for in the stage of tubulopapillary cystoma. Invasion of the lymphatic spaces of the stroma indicates malignancy. Askanazy (*Schweiz. med. Woch.*, Nov. 5, 1925).

Clinical experience has shown that cysts can assume a malignant type in some instances. As a rule, however, a pure cyst, when left to itself, re-

mains benign, and, when operated upon under strict antiseptic precautions, does not recur.

Treatment.—A serous cyst should be **aspirated** with a small trocar, this being followed by the **injection of iodine**. If suppuration occurs, or if the cyst is not cured by the injection, it should be opened and **evacuated**. **Excision** may have to be resorted to, but the fact that the walls of the cyst adhere to the adjoining tissues renders this procedure somewhat difficult.

Chronic mastitis in its later stages is often associated with the presence of cysts. A single small cyst may occasionally be satisfactorily treated by **aspiration** of its contents, but this is purely palliative. The cyst will probably recur. If the cyst is large, or if several are present, **operation** will have to be considered, since the application of X-rays is not to be advised. G. Keynes (*Lancet*, Jan. 2, 1926).

Cysts of the breast are common, and rarely undergo malignant change unless subjected to improper treatment or irritation. They are commonest in nullipara, usually between 30 and 45 years. As a rule, they are single, but may be multiple, and sometimes occur in both breasts. A history of disappearance of a tumor means rupture and absorption of the contents of a cyst. Puncture of a single cyst often results in cure, but this practice has been discontinued because of the fear of cancer. A cyst is often painful—certainly so if of rapid development. The pain and soreness are aggravated by menstruation. Palpation reveals circumscription and fluctuation; the one, when the breast is gently rolled on the chest wall under the hand, and the other, when the tumor is held against a rib and palpated with 2 fingers. Enlargement of axillary nodes is never present unless suppuration has occurred in the cyst, which is extremely rare. In **operating** for benign breast conditions the writer favors the Gailard Thomas or Warren incision along

the lower and outer periphery of the organ, with elevation of the latter so that its whole under surface can be seen and felt. The excised breast tissue should be triangular, with the apex at the center of the breast. In cases of cyst or cystic mastitis, this method will often reveal unsuspected small cysts or more extensive involvement of the breast. If so, it is best to remove the whole organ, with or without the overlying skin and nipple. J. H. Gibbon (*Atlantic Med. Jour.*, May, 1926).

DERMOID CYSTS.—These tumors are rare and may be in the skin or imbedded in the breast tissue proper. These benign cysts clinically never resemble the malignant growth, but may eventually become malignant (Bloodgood). Should the tumor become infected, it resembles an abscess. The cyst is recognized by its distinct wall and characteristic contents upon exploratory incision.

By dissection the cyst is easily separated from the surrounding tissues.

HYDATID CYST.—Hydatid cysts begin as a simple, hard, distinctly circumscribed swelling, freely movable on the subjacent tissues. The growth is slow and may remain stationary for years, never larger than a hen-egg. Should suppuration take place the hydatid membranes and hooklets may be seen with the pus. Axillary glands may or may not become enlarged. The breast becomes painful in the later stages.

Suppurating hydatids may be mistaken for an abscess, but aspiration will reveal the true nature of the disease.

Treatment.—The treatment consists of **dissecting out the tumor**; or if much glandular substance has been destroyed, partial or complete **amputation** is preferable.

SEMIMALIGNANT TUMORS. CYSTIC DISEASE, OR CHRONIC CYSTIC MASTITIS.—There is a notable absence of a well-defined tumor. Earlier writers regarded this condition as a distinct and separate disease, but more lately it has become the accepted belief that chronic diffuse mastitis and general cystic disease are one and the same. Whether the termination is by resolution or abscess, a condition of subinvolution exists.

While these growths may themselves be benign, they are believed by some observers to degenerate into a malignant growth in many instances, and by others to occur concomitantly with cancer; the former are doubtless in the right.

According to Speese, chronic cystic mastitis constitutes 13 per cent. of all breast diseases. Two types occur with equal frequency, those in which the growth is distinctly cystic, and those in which the epithelium of the cyst is hyperplastic. Histologically, the proliferative class is subdivided into those in which the epithelial proliferation occurs in the acini, those showing the presence of distinct papillæ in the cysts, and those characterized by the formation of adenomatous areas. The tendency toward malignant degeneration is greatest in the last-mentioned form. These several groups are symptomatically identical. The disease usually occurs in women approaching the menopause, though it is found at an earlier age. It grows slowly, at times rapidly. The affection is at times bilateral, is exceptionally painful, and occasionally tender on palpation. The axillary lymph-nodes may or may not be enlarged, but are not as hard as the glands characteristic of cancer.

Report of 218 cases of chronic cystic mastitis operated on at the Mayo Clinic. Of these, 11 were in males. Seventy-nine per cent. occurred in the cancer age. The condition in many instances may be considered precancerous. In cases suspicious as to

malignancy a radical operation for cancer should be performed. In cases that cannot either clinically or pathologically be diagnosed as to malignancy, conservative amputation with removal of the gland-bearing fascia is the operation of choice. E. S. Judd (Jour. Mich. State Med. Soc., Jan., 1914).

In 200 breast operations there were, for carcinoma, 108; sarcoma, 2; cyst, 47; chronic cystic mastitis, 16; fibroma and adenoma, 27. Thus, the non-malignant breast conditions requiring operation are nearly as common as the malignant, *viz.*, 45 per cent. of the 200 cases.

Chronic cystic mastitis is not so easily diagnosed as either cancer or the single cyst. There is complaint of pain or discomfort in the breast, especially at menstruation—a history rarely obtained in cancer. The area involved is usually the lower, outer quadrant, and often some induration and sometimes lobulation of the breast tissue can be felt there. These typical signs are, however, often wanting when pain, discomfort and a sense of weight are present. Many of such patients are suffering from cancerphobia, or the menopause, or both, and in the absence of some physical sign there is no reason to operate. These patients should be advised to present themselves every 2 or 3 months for examination. J. H. Gibbon (Atlantic Med. Jour., May, 1926).

As described by Syms, chronic cystic mastitis is characterized by irregular, tumor-like masses, which may be felt within the limits of the glands. There may be found one or two well-defined tumors; in fact, there may be present one or more well-developed fibroadenomata. The breast may have a very irregular contour. It is frequently hypersensitive, though actual pain is not a characteristic sign. The skin is not adherent, the nipple is not retracted, or if retracted has no special significance.

The breasts seldom attain large size. The condition is often discovered accidentally, though usually the patient has known of the existence of a growth for a long time, but thought it of no importance because of the lack of pain.

Treatment.—The treatment is, of course, governed by the nature of the growth present, but the likelihood of malignancy emphasizes the need of **surgical removal** even as a precautionary measure.

Chronic cystic mastitis is less often associated with the presence of carcinoma than chronic mastitis without cysts, so that **operation** need not necessarily be regarded as imperative. Removal of one segment of a breast, or even local excision of a cyst, may occasionally be justified, but complete local amputation of the breast is usually to be preferred. If the slightest suspicion of carcinoma has arisen, an operation must be performed without delay. Geoffrey Keynes (Lancet, Jan. 2, 1926).

MALIGNANT TUMORS.

SARCOMA.—Pure sarcoma is rarely met with; it is usually associated with other morbid conditions of the mammary tissues; hence the names *adenosarcoma*, *fibrosarcoma*, *myxosarcoma*, and *cystosarcoma*, given these growths, and which denote their associations.

Symptoms.—Clinically sarcoma may assume the type of a rather *circumscribed* tumor, which is immovable, lobulated, and firm. After a time the elevations project somewhat, and may become very soft, and finally become foci of ulceration. The malignant nature of the growth then appears and the axillary glands may become enlarged.

A second form is the *diffuse* sarcoma, which rapidly invades the en-

tire gland, but follows otherwise about the same clinical course as the first variety. In sarcomas associated with soft tumors, such as adenoma or myxoma, the tumor is less hard, and suggests the benign forms with which the sarcomatous type is combined.

Diagnosis.—From cancer of the breast sarcoma is distinguishable by the following characteristics: It does not adhere to the skin, though this may be distended, thin, and even ulcerated, owing to the size of the tumor. The entire gland is not, as a rule, affected and the nipple is not retracted. The axillary lymphatics are seldom enlarged. There is but little pain.

Mammary sarcoma occurs in young adults, whereas cancer rarely appears before the age of 45 years. It is frequently observed in men, and in them is usually of traumatic origin. It is often mistaken for an abscess and opened.

Prognosis and Treatment.—Sarcoma is ranked next to cancer as regards malignancy. It may also recur after extirpation, and may become generalized in the viscera. The fact that it does not always do so causes this variety of growth to be classed as semimalignant. It should be **removed**, including the superjacent skin. This is easily accomplished by raising the mass with one hand and including it within two semilunar incisions the tips of which meet. No diseased tissue should be allowed to remain.

Case of sarcoma of the breast in a colored girl 16 years of age. The tumor was removed and after six years there was no evidence of recurrence. Miel (Denver Med. Times, Feb., 1907).

The prognosis after removal of a mammary sarcoma must always be

a guarded one, although statistics seem to give more favorable results in excisions of the breast for sarcoma than for carcinoma. Thus, Horner's figures show 76.9 per cent. free of recurrences after two years, and ultimately 61.5 per cent. of total recoveries, but their statistical value depends entirely on whether or not the cases were all true sarcomatous tumors. The spindle-celled variety of tumor is undoubtedly the least malignant. Probably the most important element in prognosis is the rate at which the tumor has grown before operation—the more rapid that has been, the more unfavorable. In fact, clinical experience teaches that the malignancy of some sarcomata exceeds that of the carcinomata, and that early invasion of the axillary glands is an unfavorable feature. Sir George Beatson (Edinburgh Med. Jour., Jan., 1909).

CANCER.

The pathogenesis of cancer itself has been so thoroughly considered in the second volume of the present work under **CANCER** that a few additional facts concerning its occurrence in the mammary gland need alone be reviewed in the present article.

About 11 per cent. of breast tumors are said to be benign, but non-malignancy is in a much greater proportion in the early stages. The influence of transient trauma has been much disputed, but a history of injury, usually transient in nature, was obtained in 13 per cent. of the malignant breast tumors by the author. J. B. Deaver (Jour. Amer. Med. Assoc., Mar. 15, 1913).

Of 218 cases from the Mayo Clinic, 41.7 per cent. of those over 50 years of age were alive from 5 to 8 years after operation, while only 31.8 per cent. of those under 50 lived a corresponding time. The immediate hospital mortality from operation was less than 0.5 per cent. The prog-

nosis was not affected by the removal of small growths for microscopic diagnosis before the radical operation. Sistrunk and MacCarty (Trans. So. Surg. Assoc.; Jour. Amer. Med. Assoc., Jan. 8, 1921).

Two forms of cancer of the breast are met with, the *scirrhus*, or hard, cancer, in which there is excessive development of fibrous tissue, and the *encephaloid*, or soft, cancer, in which the epithelial elements play the leading rôle.

SCIRRHOUS, OR HARD, CARCINOMA.—In this variety the initial symptoms vary with the location of the primary cancerous focus. In deep-seated cancer the gland may become enlarged and hard, but not essentially deformed. The skin adheres closely to the mammary tissues, and the gland itself adheres to the mammary walls. In other cases the breast practically collapses and atrophies and the nipple becomes retracted, constituting the atrophic, or withering, form of scirrhus.

The earliest symptom of diagnostic importance is adhesions between the growth and the overlying skin—not the infiltration met with in advanced cases, but a delicate involvement, causing a faint dimpling of the skin. Often this is only visible after careful examination in suitable light. In its earliest stages, this adhesive tendency can be made to appear by grasping the breast on each side of the suspicious nodule and trying to push the skin away from the tumor. C. Rowntree (British Medical Journal, May 5, 1923).

A small swelling, especially after 30, is suspicious. An incision into or through it should show, even in small malignant growths, a cartilaginous resistance to the knife, a hard edge, a cupping of the surface, with the appearance of an unripe pear. W. H. Battle (Lancet, Jan. 5, 1924).

In still another type the cancerous process affects a certain part of the breast only, and thence invades the whole gland by throwing out fibrous bands or strips, which radiate through the organ in all directions. The surface of the breast may then assume various types of irregularity, with promiscuously distributed undulations.

The tumor may be essentially cutaneous at first and subsequently invade the deeper tissues. It then appears in the form of irregularly disseminated *plaques* or hard, superficial areas, which unite and may involve a large portion of the superficial tissue. The skin appears as though tanned, and is hard, rough, thick, and red. This scirrhus transformation may gradually affect the whole anterior portion of the thorax, which thus appears to be topped with a sole-leather-like covering; hence the name "*en cuirassé*" given this type of cancer. Sometimes the disease appears in the form of nodules varying in size from that of a cherry to a millet seed. These nodules are hard and vary greatly in number. They may, however, remain in the same condition a long time if let alone, but frequently ulcerate. If removed they rapidly recur. They are due to penetration of the cancer-cells into the perivascular lymph-spaces of the cutaneous vessels. When scirrhus of the skin follows upon a deep-seated cancer, similar nodules may develop around the edge of the cancerous ulcer. Their appearance indicates a tendency to spread and to become generalized.

Scirrhus, or hard, cancer, when left to itself, transforms the whole breast affected into a stone-like mass. Into this the nipple is more or less

drawn by contraction of the milk-ducts through infiltration of the latter with young cells and subsequent metamorphosis into fibrous tissue. If the cancerous focus is far from the nipple, the latter may only be somewhat distorted through irregular tension of the skin.

Deep or superficial ulceration may occur, which differs greatly from that observed in epithelioma of the breast. The ulcer resembles a crater with irregular, hard, everted edges, and whose base is covered with foul, unhealthy granulations, giving off a thin, offensive discharge. Such ulcers are apt to bleed, and severe hemorrhages may occur. The axillary glands become involved early; but their detection at first requires careful examination. They gradually enlarge, and by pressing upon the surrounding vessels and nerves may give rise to edema of the arm or to neuralgic pains. The entire lymphatic system of the trunk is exposed to contamination; hence the visceral complications often witnessed.

Metastasis to bones occurred in 67 out of 1985 cases. The 67 comprised: Pelvis, 26; femur, 23; lumbar spine, 21; ribs, 18; dorsal spine, 11; cervical spine, 4; clavicle, 4; scapula, 4; sacrum, 4; cranium, 2; tibia, 1; sternum, 1. Multiple bone involvement existed in 43. In patients complaining of "rheumatic" or "sciatic" pain, the possibility of metastasis to bone should be considered. Meyerding, Carman and Garvin (*Radiology*, Dec., 1925).

Suffering only becomes serious when the tumor has reached a certain size. Pain of a stinging or burning character is sometimes complained of; involvement of nerves often causes it to be neuralgic and persistent, especially in the shoulder and arm. The

ulcerative process, the general toxemia incident upon the presence of the purulent mass, and the mental sufferings of the patient bring on exhaustion, which finally ends in death.

Pain in the breast is not, taken alone, of diagnostic value; nor is a painful scar an indication of recurrence. Recent retraction of the nipple, without a history of lactation, points to cancer. Lesions of the nipple suggesting Paget's disease, not healing in a few weeks after simple measures of cleanliness, call for complete breast excision. A breast larger than the other, but retaining its symmetry, is not suspicious. Differentiation of breast lesions depends mainly on palpation. Bloodgood (*Jour. Amer. Med. Assoc.*, Mar. 25, 1922).

ENCEPHALOID, OR SOFT, CARCINOMA.—The encephaloid variety of mammary cancer, though less often met with than the scirrhus, is nevertheless common. It always starts in the gland itself, and only affects the skin at a later period. Its onset is insidious. It may have existed for some time unperceived by the patient. A hard tumor located in the gland is first noticed; this may be free from surrounding tissues or fixed, according to the time it is detected. It may also present nodules varying in density owing to the presence of cysts and sanguineous infiltration. At first the skin is free and traversed by unusually prominent bluish veins, some of which finally become varicose; spots of redness then appear, the precursor of adhesion of the cancerous mass to the skin. This occurs at an early stage, and is caused by infiltration of the cancerous elements into the tissues. The whole tumor then becomes a reddish, fluctuating mass, which soon degenerates and becomes fun-

gous; it then bleeds easily when touched, and gives off a foul odor. Burning and shooting pains, which are more severe and appear earlier than in scirrhus cancer, occur, and steadily increase in intensity. Retraction of the nipple also occurs, and engorgement of the lymphatics can be detected at an earlier date.

The ulceration differs essentially from that of scirrhus. Instead of being surrounded with a harder border, forming a crater-like cavity, it assumes the aspect of a large fungous sore. The least touch causes it to bleed, and hemorrhages are much more frequently observed than in scirrhus, but fortunately are arrested with less trouble. Cachexia also appears earlier. All the acute symptoms are aggravated, and complications in remote organs are more frequent.

DIAGNOSIS.—The anxiety caused by a growth in this region renders a careful differential diagnosis of unusual importance.

The first question to be determined is whether the tumor is benign or malignant. To determine the exact nature of a tumor at the very onset is often impossible, but this difficulty gradually decreases as time progresses. Still, there are at all times landmarks upon which the surgeon may base a guarded opinion even early.

As a rule, benign tumors occur before the age of 35 or 40, while the malignant growths are more frequently met with after that age. Again, the evolution of the neoplasm is much more rapid in malignant tumors than in the benign. The latter usually remains free or detached, and, if at all superficial, can be rolled under the finger, indicating the ab-

sence of adhesions. In malignant tumors, on the contrary, adhesion to all the surrounding tissues becomes at once evident, their limits, even in the beginning, being practically indefinable, while later on the cutaneous and all the underlying tissues become incorporated in the tumor.

As emphasized by Deaver, lancinating pain is not an early symptom, though it is common in the later stages. The favorable time for operation is when there is a symptomless, freely movable lump in the breast. Absence of attachment to the pectoral fascia does not indicate non-involvement of the fascia, which, as well as the muscles and intramuscular lymphatics, may be involved before adhesion occurs.

Minute depressions in the skin, resembling those of an orange, may occur over a cancer of the breast. The arm must be abducted to ascertain the movability of the tumor on the pectoralis major. The arm is then adducted and the hand introduced under the muscle to palpate glands on the edge of the pectoralis minor. The axilla as well as the edge of the sternum on the opposite side and the intercostal spaces may contain metastases in lymph glands. Enlarged glands, however, are not always cancerous. Paget's disease of the nipple is due to cancer and bleeding from the nipple is frequently an indication of it. Steinthal (Munch. med. Woch., July 11, 1924).

The density of the growth and the aspect of the skin also afford a clue. Benign growths are usually soft and elastic when pressed upon, while malignant neoplasms are hard and lumpy. The skin retains its softness and usually rides freely over the benign tumor, while over a malignant one the skin becomes abnormal and assumes a leathery aspect.

In benign growths the nipple usually remains free or merely distorted by the change in shape of the breast.

In cancer it is drawn into the organ and held fast in that position by fibrous bands.

The lymphatic glands of the axilla rarely, if ever, become enlarged in benign growths; if they do at all, the enlargement is slight. In malignant growths they are always more or less enlarged, and steadily increase in size as the disease progresses.

Benign tumors very seldom cause inconvenience to the patient except by their volume and their weight. Malignant tumors, on the other hand, are attended by more or less pain, usually of a lancinating character. The suffering becomes more acute from day to day.

Ulceration sometimes occurs in benign tumors through pressure, but only when the growth is very large. The edges of the ulcerated portion remain thin and free, and there is no fetid or sanious discharge. In cancer, as stated, ulceration is one of the salient features and is characterized by marked foulness. The general health usually remains good in benign tumors. In malignant tumors the patient soon becomes cachectic and shows marked evidence of deterioration. The edema of the arms and the complications alone belong to the malignant types of growth.

A scanty, thin, bloody discharge is suggestive of carcinoma, and thick granular discharges always suggest malignancy. A bloody discharge unless it can be shown to come from an intracystic papilloma should cause the entire removal of the breast. A bloody discharge is now and then seen in connection with abnormal involution and this may also occur together with retraction of the nipple, though no malignancy has yet developed. Rodman (Jour. Amer. Med. Assoc., Mar. 18, 1911).

The only hope of cure in cancer of the breast is a **radical operation**; a large proportion—32.86 per cent.—of patients operated on by the radical method pass the 3 year period, and 23.77 per cent. the five year period. J. H. Jacobson (Ohio State Med. Jour., Sept., 1918).

Sections of female breasts showed that cancer can and does begin in cysts, and that it gives rise to typical microscopic appearances of this mode of origin. The writer advises **removal** of every breast which is obviously clinically cystic, even if only a single cyst is present. G. L. Cheatele (Brit. Jour. Surg., Oct., 1920).

Treatment.—Internal remedies innumerable have been proposed as specifics, but time has in all demonstrated their worthlessness in true cancer.

Even the local methods, topically or hypodermically employed, and which will be described at the end of this article, (see also CANCER, Vol. II.) are open to serious objections, and should, therefore, only be resorted to in inoperable cases or where the patient, through fear or for other reasons, will not allow the use of the knife. The surgeon must, therefore, choose between the palliative method, which resolves itself into reducing the patient's sufferings during her gradual progress toward death, and the radical method, which gives her, if the tumor is not too far advanced, a good chance to recover. Especially is this the case since greater freedom has become the rule in the removal not only of cancer of the breast, but of the contaminated glands. Indeed, nowadays few operations for well-developed cancer can be considered radical unless removal of the primary growth is accompanied by prophylactic extirpation of its tributary lymphatic areas.

Review of the results of 609 cases of cancer of the breast operated upon at the Mayo Clinic, including 2 in males. The authors were able to trace 514. Of these, 248 were known to be alive from 2 years to 11 years and 4 months after operation. Thirty-seven of these were known to have recurrences. There was a percentage of 32.5 alive without recurrences more than 10 years; 39.8 alive more than 5 years, and 44.7 living more than 3 years.

On the whole, the functional results were very good, most of the patients reporting that their arms were all right. Pain in the arm was usually complained of shortly after operation, but in most cases disappeared within 2 weeks. Swelling and edema were occasionally marked, either primarily, due to thorough removal of the lymphatics, and persisting until collateral circulation in the lymphatics was established, or as a secondary edema several months or years after operation, and due to a recurrence in the remaining lymphatics. Metastasis may occur many years after the operation, though in the great majority it will appear in the first few years if at all. Judd and Sistrunk (Surg., Gyn. and Obst., Mar., 1914).

Attention called to *traumatic fat necrosis*, which is easily confused with cancer. All the author's cases were in corpulent women of cancer age traumatized over the affected breast 3 weeks to 10 years before appearance of the lump. Pain was absent, the tumors all extremely hard, with the nipple retracted in 1 out of 5 cases. In 4 it was fixed to the skin and in 2 to the deep structures. Lymph-nodes were not involved. The mass rapidly increased in size. **Local removal** is justified if a proper gross diagnosis can be made in the operating room. Should the gross examination reveal carcinoma **complete amputation** may then be performed. B. J. Lee and F. E. Adair (Surg., Gynec. and Obst., Apr., 1922).

Among 255 cases of breast tumor, there were 126 cases of malignancy, comprising carcinoma, 120; sarcoma, 3;

epithelioma, 1, and malignant cysts, 2. The average age in the malignant cases was 49.2 years. The youngest patient with carcinoma was a married woman aged 27. Nine cases with recurrent carcinoma averaged 44.1 years, or 5 years below the average of the primary cases; this bears out the observation that the younger the cancer patients, the harder they are to cure and the more likely it is to recur. In $\frac{1}{3}$ of the malignant cases there was a family history of cancer. The average duration of the malignant tumors before operation was 33 months, the shortest being 1 week and the longest 42 years. Excluding the latter case and the next longest, 30 years, the average preoperative duration was 26 $\frac{1}{2}$ months. Operation was performed in 103; in 19 others, or about 1 in 5, the condition was considered inoperable. In 20 per cent. there was no palpable metastasis; in 60 per cent. there was axillary metastasis only; in 20 per cent. there was axillary and other metastasis. Ten cases were ulcerating. Three were in lactating breasts, which decreases the chances for cure to almost *nil*. There were 5 deaths in the hospital following operation—2 from embolism and 1 each from infection, pneumonia and diabetic coma—a primary mortality of 4.2 per cent. In operated cases there were 5 to 11-year cures in 45.7 per cent.; 3-year cures in 58.3 per cent., and 1-year cures in 64.2 per cent. Inoperable patients lived, on an average, 9 months after consultation. The entire course of the disease in the untreated cases averaged 25 $\frac{1}{2}$ months. W. D. Haggard and H. L. Douglass (Jour. Amer. Med. Assoc., Feb. 17, 1923).

Report on 98 cases of *bilateral mammary cancers*, simultaneous in 11 and consecutive in 87. Bilateral lesions occurred 154 times among 3132 breast cancers, i.e., in 4.9 per cent. After 1720 operations for unilateral cancer, 31.6 per cent. of patients were alive 5 years later, while of the 87 patients with consecutive bilateral operations, 54 per cent. were alive 5 years after the first operation and 24.1 per cent. 5

years after the second operation. Thus, the extreme pessimism regarding the final results following operations for bilateral lesions does not seem to be justified. The second cancer, in probably a large number of patients, is a primary growth, entirely independent of the first one. McWilliams (Ann. of Surg., July, 1925).

Tumors of the *male* breast constitute between 1 and 2 per cent. of all breast tumors. Trauma, especially occupational, seems an important factor in male breast cancer. Direct involvement of fascia and muscle is very common. Radical operation is just as necessary as in the female, the prognosis being, however, probably better. K. Speed (Ann. of Surg., July, 1925).

A discharge of serum or blood from the nipple, formerly considered evidence of malignancy, is not rare after the menopause, especially if it is the result of surgery, radium or the X-rays, and is of no serious significance; if, however, it is accompanied by ulceration of the nipple or a mass under it, operation is indicated. J. H. Gibbon (Atlantic Med. Jour., May, 1926).

The results of the *older* operations, *i.e.*, prior to earlier and more radical removal, gave the following percentages of local recurrences: Billroth, 85; Czerny, 62; Fischer, 75; Gussenbauer, 64; Volkmann, 59, and Gross, 68; by present-day methods, in which *timely* and *thorough* eradication of the growth is the rule, the recurrences may be as low as 20 per cent.

Where the average case, *i.e.*, cases in the various operable stages of the disease, are thoroughly treated surgically, the chances of permanent recovery have also been greatly enhanced, even when late recurrences are taken into account.

Recurrence in the lung or pleura occurred in 3 out of the writer's 115 operated cases of breast cancer, these 3 constituting $\frac{1}{3}$ of the total of 9 known recurrences in this series. Such

recurrences often develop rapidly, irrespective of the structure of the growth. He now tries to obviate this complication by bringing about a copious serous discharge, after removal of the breast and connected glands in one mass, by inserting several layers of gauze between the deep wall of the wound and the skin flaps. Deep X-ray exposures, with the rays directed tangentially, so as not to act directly on the lungs and pleura, are also given. Delbert (Neoplasmes, Oct., 1924).

Among 653 cases operated for breast malignancy, recurrences were found to have occurred in 35 per cent. The fact that in over $\frac{1}{2}$ of these the recurrence appeared first in the operative area suggests that the primary operation failed to remove all the involved tissue. Eleven patients, or 1.7 per cent., died in the hospital during or after operation. Of the scirrhus carcinoma group, forming 58 per cent. of the whole series, 37.5 per cent. lived over 3 years and 10 per cent. over 7 years. In the carcinoma simplex group, the corresponding percentages were 32 and 16.2, and in the medullary carcinoma group, 38 and 21. The most favorable 5-year period for operation from the standpoints of duration of life and delay of recurrence is between the ages of 50 and 54. Early recurrences are more common in young patients and late ones in older patients; this supports the theory that carcinoma is more malignant before than after the menopause. A. C. Perry (Brit. Jour. of Surg., July, 1925).

As to the actual number of cures obtained by the *older* methods, Billroth (1876) claimed 4.7 per cent. of cures; Küser (1881) 21 per cent.; Koenig, 23, and Bergmann, 39. Gradually, as the malignant growths and their extensions were removed with increasing thoroughness, however, we find the average of Rötter, Helferich, and Watson Cheyne's cases (1896) to reach 49.5 per cent. Watson Cheyne found that, while in a collec-

tion of 1491 cases, obtained from various sources and operated upon by older methods, 14 per cent. had been cured, 11 operated by newer methods had yielded 34 per cent. of cures. Bloodgood, 1913 and 1914, from a series of cases at the Johns Hopkins Hospital, reported from adenocarcinoma, all cases, 76 per cent. of cures. Early cases, when the lump in the breasts was of such short duration that none of the signs of cancer were present, gave 100 per cent. of cures; late cases, 64 per cent. of cures.

In the more malignant forms of cancer of the breast—medullary and scirrhus—the results were even more striking: All cases, cured, 36 per cent. Early cases cured, 85 per cent. Late cases cured, 33 per cent. The improvement from 35 per cent. in 1908 to 42 per cent. in 1913 was entirely due to an increase in the number of early cases, since in those five years there was no improvement in the surgery of the mammary gland.

In 1923 Primrose reported 44.4 per cent. of 45 cases with five-year cures after radical operation. Among 11 "early favorable" cases, without glandular involvement, there were 91 per cent. of cures; among 13 "favorable" cases, with glands slightly involved, 61 per cent., and among 21 "average" cases, with glands markedly involved, 9 per cent.

Unfortunately, some cases are not seen sufficiently early to warrant operative procedures. Glandular involvement has often been allowed to extend to the axillæ, when the chances of a successful issue are reduced. These become inoperable cases, however, when scattered cancerous tubercles are met with over large areas, indicating extensive infiltration of the

skin,—i.e., undefined limits; or, when the cancer has assumed the *en cuirasse* type, and has so progressed as to involve a large part of the surface. They become especially so when the internal viscera—the liver, the lungs, etc.—show indications of metastasis. Great and persistent edema of the arm is considered as a contraindication, but it should not stand as such in all cases.

Analyzing 218 cases treated at the Mayo Clinic, the writer found that the axillary glands were involved in 60.5 per cent., showing that the majority of patients come to operation late. Death may be expected within 5 years if the glands are involved at the time of operation. The growth proved about 3 times as frequent in the upper outer quadrant of the breast as in any other quadrant. In 97 cases local recurrences occurred. Of the 218 patients, 2.7 per cent. died within 6 months; 21 per cent. by the end of the first year; 34.9 per cent., of the second year; 42.2 per cent., of the third year, and 49.1 per cent., of the fourth year. Only 2.3 per cent. died after 5 years; 85, or 39 per cent., were alive at the end of this time. Sistrunk (Jour.-Lancet, Feb. 15, 1922).

Among 83 cases with radical extirpation, the patients with glandular involvement were living after 3 years, 5 years and longer after operation in 20.34, 15.79 and 14.04 per cent. of cases, respectively. In patients without glandular involvement the corresponding percentages were 70.83, 66.67 and 66.67. Thus, the prognosis depends markedly upon the condition of the glands. E. Dahl (Norsk Mag. f. Lægevid., Nov., 1925).

A class of cases in which forbearance should be the rule is that occurring in old women, in whom a cancerous growth may, without giving rise to serious suffering, extend over several years—ten to twenty sometimes. An operation in such cases

would soon be followed by recurrence and earlier death.

The most important contraindication to operation, according to Finsterer, is distant metastasis to the internal organs. A second contraindication is the absolute fixation of the tumor to the thorax, though operation has been done on a few of such cases. The third contraindication is the spreading of the cancer in lentil-like masses over the chest or cancer *en cuirasse*. However, the author's series of 520 cases presents 9 exceptions to this. In 1 of these cases the woman was still living 7 years after the operation and did her own housework. The general condition of the patient, the age, and the presence of other diseases must be considered, the latter only in reference to the degree of development. The final contraindication is furnished by the presence of involvement of the supraclavicular lymph-glands. This, however, is a debated point.

A primary inoperable breast carcinoma is one in which one or more of the following factors are present: Fixation of the breast tumor to the chest wall; involvement of the supraclavicular nodes; definite involvement of the opposite axillary nodes; diffuse subcutaneous nodules; diffuse inflammatory carcinoma involving a considerable skin area; chest metastases, pleural or mediastinal; more remote metastases. In this group of cases the writer has seen little palliation from operation. Patients' lives were not prolonged, their pain was not relieved, and they had the additional discomfort incident to operation. E. A. III (Jour. Med. Soc. of N. J., Aug., 1924).

• Encephaloid growths occurring in young women seldom warrant operative procedures when at all advanced. Their evolution is extremely rapid in such cases, and excision is almost always followed by recurrence.

Barring the above-mentioned features, **extirpation** is indicated in every case. Many prominent surgeons, indeed, recommend the removal of all benign growths, since they often be-

come the foci for the development of malignant neoplasms. Even when relapses occur successively, the operation prolongs life, tranquillizes the patient, and greatly decreases her sufferings. When in addition the increasing ratio of cures by modern methods is considered, the duty of the medical attendant becomes imperative.

The prohibitive features enumerated having been eliminated by a careful examination, the supraclavicular spaces and axillæ should be carefully examined for enlarged glands. When enlarged supraclavicular or axillary glands are detected their influence upon the surrounding tissues is a good gauge as to their size. The presence of pain, slight edema, stiffness, etc., should be carefully looked into, and, if none of these are complained of or detected, the chances that the glandular involvement is slight are very great. Some surgeons have recommended an exploratory incision under anesthesia to ascertain that the glandular involvement before operating is not excessive. This is unnecessary, since the need of such a step proves that the case is an operable one.

Malignancies of the breast never begin with pain, and when pain is a symptom of cancer no expert is required to diagnose the condition. The dimpling sign of malignancy is obtained very early. Upon lifting the breast from below or compressing it between 2 or more fingers, dimpling readily follows, while in the non-involved breast the convexity will remain or be exaggerated. This dimpling can also be seen by either direct or oblique inspection, and by feeling carefully over the dimple one obtains the sense of hardening or tumor. Many patients with normal breasts show single or bilateral retracted nipples. In the retracted nipple of malignancy,

however, eversion is usually impossible, while in the normally retracted nipple eversion is quite possible in the great majority. Axillary adenopathy, to be found readily on palpation, usually requires an exceptionally enlarged gland or an exceptionally thin subject. In relation to operative justifiability, one cannot be too careful, in the readily palpable tumor, in the search for metastases—those of the mediastinum or lungs, characterized by a dry cough, or of the bones, with facial, intercostal or sciatic pains. J. F. Erdmann (Amer. Jour. Med. Sci., Dec., 1924).

Operation.—The most effective procedure is that of Halsted, who contends that the pectoralis major muscle entire, except its clavicular portion, should be excised in every case of cancer of the breast, because the operator is enabled thereby to remove in one piece all of the suspected tissues. J. Collins Warren also emphasized the importance of thorough removal of all suspicious tissues, including a large margin of the cutaneous covering of the breast, a careful deflection of the edges of the wound, removal of the subcutaneous fat for a considerable distance around the mammary gland, the removal of the pectoral muscles, and a minute and painstaking dissection around the sheath of the axillary vessels.

The breast should first be carefully cleansed and aseptized as far as possible and the axilla shaved and treated in the same manner. The incision is then begun at the anterior axillary fold, and, descending as an ellipse embracing the whole gland, is then brought back to the starting point. The skin and fat of the regions traversed should be penetrated down to the muscular tissues beneath, the organ being then detached from below

upward, *i.e.*, progressing toward the axilla.

The supraclavicular region was almost invariably cleansed out by Halsted at this stage, and he found that removal of the supraclavicular fat and lymphatics is best done from within outward and from below upward. The subclavian vein being the starting point in the dissection of both the infraclavicular and supraclavicular regions, it is unnecessary to remove the clavicle and useless to divide it. By elevating the shoulder the clavicle can be raised an inch or more away from the first rib. The fingers can be passed from the supraclavicular to the infraclavicular and to the subscapular regions under the clavicle, and any fat in the latter region, near the internal or the posterior border of the scapula between the serratus magnus and subscapular muscles, which could not be drawn out through the neck, removed. To excise the supraclavicular tissues a vertical incision is used parallel with the sternocleidomastoid muscle near its posterior border; a few of the posterior fibers of this muscle are divided and the junction of the internal jugular and subclavian veins is exposed. At the angle of junction of these veins the dissection is begun. The omohyoid is divided at its tendinous part, the two bellies of this muscle being drawn out of the way. The supraclavicular fossa is cleansed out or stripped, with very few exceptions, at the primary operation. The rule should be to operate on the neck in every case. The minor as well as the major pectoral muscle is removed, the insertion of the major, and then its origin and the origin of the minor, being divided before the sub-

clavian vein is exposed, first at its inner part, and the axilla stripped of its contents and its anterior wall at one time from within outward and from above downward. The mass to be excised must always be circumscribed with a circular or an oval incision, and an additional cut made to expose axillary and jugular veins. The operation is performed in an absolutely bloodless manner. In all cases the wound is grafted immediately; this is done by cutting grafts from the patient's thigh as large as or larger than one's hand. A single one of these large grafts may be enough to cover the raw surface. In cutting a graft of this kind the skin is made tense by a board which the operator slides along the thigh just in front of a large amputating knife or catlin. The graft is spread, raw side up, on a piece of rubber tissue, and from the latter is readily transferred to the breast wound. It is finally covered with silver foil and tissue-paper, and need not be looked at again for two or more weeks.

The incision down the arm, made shorter and shorter, was finally abandoned. The vertical cut to the clavicle is made as short as feasible, and when considerable skin has been removed above is omitted. Not infrequently the only incision of the skin is the circular one surrounding the tumor, but, as a rule, the one or the other of the vertical incisions has been made. By means of the two vertical incisions, one above and one below, the dissection of the axilla is, of course, facilitated. Thus the triangular flap has been definitely abolished. The skin of the outer flap between the two vertical incisions is utilized primarily to cover completely, without any tension whatever, and redundantly the vessels of the axilla. The edge of this flap is

stitched by interrupted, buried sutures of very fine silk to the fascia just below the first rib in such way that the skin partly envelops the large vessels. Then, along the entire circumference of the wound, the free edge of the skin is sutured to the underlying structures of the chest wall, the wound being made as small as desirable in the process of closure, and tension on the upper or axillary part of the outer flap assiduously avoided. Considerable traction may, however, be exercised on the mesial flap and on the lower portion of the outer flap. Whatever the size and shape of the grafted defect, it should usually extend to the top of the axillary fornix. Thus the thoracic or inner wall of the apex of the axilla is always lined with skin-grafts. The advantages of skin-grafts are that an almost unlimited amount of skin may be removed, and from his experience the results have been better the larger the areas of skin taken away, and the wider berth given the tumor. Skin-grafts present a definite obstacle to the spreading of cancer metastasis, as the growth does not tend as much to invade the grafted area. W. S. Halsted (Jour. Amer. Med. Assoc., Feb. 8, 1913).

Experience has convinced the writer that in many instances the sole reason for recurrence is insufficient removal of skin, the surgeon being too much preoccupied, as a rule, in leaving enough skin to render possible immediate union of the wound margins. By using a flap consisting of skin from the back, as well as large sections of the latissimus dorsi and teres major, free excision of skin is permitted, viability and high resisting power of the covering of the wound is insured, and the formation of a linear scar in the axilla, with consequent limitation of movement and compression of veins, is avoided. The writer advocates the use of his method of closure in all cases of breast cancer in which a radical operation is not contra-

indicated. Tansini (*Presse méd.*, Jan. 3, 1914).

In recent years there has seemed to be a diminution in the ratio of cancer as compared with benign tumors of the breast. Bloodgood, on the basis of 1577 cases recorded in the surgical pathological laboratory at the Johns Hopkins Hospital, gives the following percentages of benign lesions:

From 1889 to 1900	32
From 1900 to 1910	41
From 1910 to 1913	47
From 1913 to 1915	59

Bloodgood has also urged that inoperable cases are distinctly on the decrease. In 74 breast operations the writer found 26 to be benign. J. H. Jacobson (*Ohio State Med. Jour.*, Sept., 1918).

In patients admitted to the Harper Hospital, Detroit, the average duration of the tumor before operation decreased from 16½ months in 1914 to 10 months in 1920. Saltzstein (*Amer. Jour. Med. Sci.*, Mar., 1923).

When such radical measures are not required, and a simpler operation is warranted by the limits of the tumor, the following procedure may suffice: An incision is made from the axilla, but anterior to it, extending downward and around the tumor, the latter being included in the ellipse formed, and meeting the starting point. Even if the growth be exceedingly small, a wide margin should be removed with all suspected tissue. The knife should penetrate clear down to the muscular aponeurosis, from which the mass can easily be detached, but if the aponeurosis is adherent it must be removed. If any muscular fibers also show adhesions, the Halsted operation should be resorted to. The vessels should be rapidly caught to avoid hemorrhage as the operation proceeds.

Examination of the axillary ganglia

is warranted in all cases, and their careful dissection is always indicated when there is the least suspicion that they may be involved. They are unmistakably so in over 60 per cent. of cases.

The transverse incision of Stewart is favored by the writers, as the resulting scar is well placed and does not encroach on the shoulder or arm. The direction of the incision facilitates sliding upward of the lower flap so that skin-grafting is rarely necessary. The pectoralis minor is usually preserved, either by division and resuture, or better, by retraction for axillary dissection. Block dissection is used from above and within downward and outward, following the plane beneath the pectoralis major and removing the sheaths of the pectoralis minor and serratus magnus. The axilla is drained through a stab wound. The supraclavicular glands are not excised; if the disease has involved this group the prospect of a radical cure is slight. Excision of a portion of the sheath of the rectus is done only when it comes naturally in the field of a wide block dissection. A wide oblique dissection of subcutaneous fat is made well out beyond the edge of the skin incision. In doubtful cases the tumor is completely excised with a safe margin of adjacent tissue, and immediately cut and inspected by a pathologist and the surgeon. In the majority of malignant tumors, gross inspection of the cut surface is quite sufficient for diagnosis; if doubt exists, the result of a frozen section is awaited, to be interpreted along with the gross section, the presence or absence of encapsulation, and the general clinical picture. Peck and W. C. White (*Ann. of Surg.*, June, 1922).

To avoid metastasis the writer keeps as far away as possible from the strip of skin under which the superficial and deep lying lymph vessels pass from the mammary gland to the axilla, since it is along these particular lymph vessels that metastasis is likely to occur. Czirer (*Zent. f. Chir.*, Jan. 6, 1923).

The two edges of the wound should then be sutured, after having placed a drain at each end of the wound. The whole may then be dusted with an antiseptic powder or a dry sterile dressing applied and covered with a thick layer of antiseptic absorbent cotton, held in position by adhesive strips or a broad bandage tightly fastened around the chest. The dressing should not be removed until the third or fourth day, to remove the drains and sutures. These may be replaced by strips of linen impregnated with iodoform collodion.

Case of subsidence of an inoperable mammary cancer after **bilateral oöphorectomy** (Beatson's operation) in a nullipara of 45, who had been menstruating regularly. The edema of the arm, 2 deep ulcerations, and enlarged, hard axillary glands disappeared in 2 months and the general condition was completely transformed. Reynès (Bull. de l'Acad. de méd., Mar. 22, 1921).

Treatment of Inoperable Cases.—

When the growth cannot be removed, palliative measures must be adopted. The organ must be relieved of all pressure, and the movements of the corresponding arm restricted as much as possible. The use of **morphine** and **atropine** hypodermically in such cases is fully warranted, the object being to curtail suffering, even if very large doses have gradually to be reached. Locally, **boric acid**, directed over the growth, and a solution of **acetate of lead**, 20 grains (1.3 Gm.) to the ounce (30 c.c.), sprayed over it, are useful procedures. Local applications of solutions of the **extract of opium** or **belladonna** sometimes quiet the suffering. **Chloretone** may be used for the same purpose.

Bernart has recommended, as a curative measure in inoperable cases,

interstitial injections of a solution of **salicylic acid**, 15 minims to 1 dram (1 to 4 c.c.) of a 6 per cent. **alcoholic solution** being used after strict antiseptis. From 10 to 15 injections are said to produce considerable alleviation.

Hassel, of Nordhausen, has used **injections of alcohol** for many years in inoperable cancer. He believes cure could be effected in cases of breast cancer by surrounding the breast with cicatricial tissue by means of alcohol injections. It is preferable, however, to extirpate the organ and treat recurrences by the injections. In this manner he obtained radical cure in a case declared inoperable by Volkmann. Vulliet, Kuh, Young, and others have also obtained good results from this method. Hassel used alcohol diluted $\frac{1}{2}$ or even more with very sensitive patients. One, or at most two, injections are made at a time, drawing the breast out and inserting the needle so as to cause the alcohol to penetrate into the retromammary cellular tissue beyond the middle of the gland. The contents of the syringe should flow out gradually on gentle pressure of the piston. If there is resistance it should be withdrawn a little and the point reinserted sidewise in another direction. In this manner the retromammary space is filled with the alcohol. From 4 to 10 c.c. (1 to $2\frac{1}{2}$ fluidrams) are used for small tumors and 10 to 20 c.c. ($2\frac{1}{2}$ to 5 fluidrams) for larger ones. One must be careful to keep well in the space behind the tumor. After the needle is first introduced it should be withdrawn to see if any blood flows out of the needle-hole. If it does, the syringe must be cleansed and inserted in another place. The injections are made once or twice a

week at first, and then later once in two or three weeks. These injections are, unfortunately, rather painful.

The local use of **zinc chloride**, after devitalizing the sensitive tissues with potassium hydrate, has been revamped with success by Strobell.

Case of ulcerating epithelioma or rodent ulcer of the breast in a woman of 60, with destruction of the nipple and invasion of the surrounding areola, in which administration of 3 capsules daily, each containing 0.02 Gm. ($\frac{1}{2}$ grain) of powdered **thyroid** and 1 Gm. (15 grains) of powdered **mammary gland**, $\frac{1}{2}$ hour before meals, was followed in 11 weeks by complete healing of the ulcer. Naamé (*Presse méd.*, Dec. 8, 1923).

Another, more widely used method which seems to have afforded encouraging results is the use of the **Röntgen rays** or **radium**. There is no general agreement, however, as to their exact value or indications, either in operable or inoperable cases.

The application of the **Röntgen rays** will at times cause a disappearance of both small and extensive areas of both recurrent and metastatic carcinoma. The additional administration of **thyroid gland** in small doses, as first recommended by Sajous in 1907, seems to aid materially in cure of the disease. Pfahler (*Surg., Gyn. and Obst.*, Jan., 1914).

The writers recommend preliminary **radiation** covering the mammary, supraclavicular, and axillary regions twice during a period of 2 weeks, followed within a few days by a complete surgical operation, and 2 or 3 weeks later by thorough radiation over all these areas. In primary inoperative carcinoma, a 40-minute exposure is given at 40 cm. distance, with a 6 mm. filter, 9 in. parallel spark gap, and 5 ma. current over each area, and within a week the exposures are repeated for 25 minutes. After 2 weeks, if the patient cannot be operated upon,

radium needles are introduced into the tumor masses, sufficient to cause complete destruction. This is followed again in about 2 weeks with further radiation, and so on until the disease completely disappears. Pfahler and Widmann (*Jour. Me. Med. Assoc.*, Apr., 1922).

Radium used postoperatively and in recurrences has given results which justify its use; but the most successful results will be obtained when radium is used as a routine measure, preoperatively. It disintegrates the tumor mass and cell nests and forms fibrous tissue masses which block off the lymphatics. He uses a transfixion needle, 15 cm. long, containing 33.33 mgm. of radium. G. S. Willis (*N. Y. Med. Jour.*, Apr. 18, 1923).

After postoperative prophylactic irradiation the author witnessed freedom from recurrence in 55 per cent. of 96 cases after 3 years, and 39 per cent. in 75 cases after 5 years, as compared with 32 per cent. and 28 per cent. in his cases in which postoperative irradiation was omitted. When *intensive* postoperative irradiation was employed, however, he had 47 per cent. of recurrences the first year—as many as in the non-irradiated cases. J. C. Lehmann (*Zent. f. Chir.*, Feb. 16, 1924).

A skiagram of the chest is necessary, as some patients unexpectedly show pulmonary or mediastinal involvement even with a small breast lesion. If the patient is a good operative risk, a radical breast and gland enucleation is the immediate imperative step. About 10 days after operation a heavy **radium** treatment is given in an effort to destroy any cancer cells left behind, 5 or 6 portals being chosen along the line of incision and 1 Gm. at $\frac{1}{4}$ inch applied for 10 to 12 minutes to each. The axilla and supraclavicular spaces are radiated, the equivalent of 5 or 6 Gm. at 2 inches being given for an hour. The patient is kept under observation at increasing intervals for several years, and treated with radium if there are recurrences. Bad operative risks, patients who refuse operation, and cases with metastasis have radium left as their one

hope. H. A. Kelly and R. E. Fricke (Surg., Gyn. and Obst., Mar., 1924).

Of 7 cases of breast cancer with bone deposits, 2 were given **X-ray** treatments, with resulting marked improvement of general health, prolongation of life and relief of distressing symptoms. Giles (Amer. Jour. of Roentg., Nov., 1925).

The writer disapproves of pre-operative radiation and employs **radium** only for the prevention of recurrences after operation. He favors the French procedure of repeating the exposures for several days. Recurrence in 2 years occurred in only 1 out of 10 cases thus dealt with. Tománek (Casop. lek. cesk., Dec. 12, 1925).

[See also **CANCER**, Vol. II.]

TUBERCULOSIS OF THE BREAST.

There are two characteristic varieties of mammary tuberculosis: the *disseminated nodular* form and the *confluent*.

The *nodular* variety is characterized by the development of single or multiple hard nodules, only slightly painful and at first non-adherent to the skin. The process is exceedingly chronic, and only after the lapse of several years do the nodules break down and form suppurating fistulæ.

The *confluent* variety is characterized by a more acute onset, greater pain, and rapid enlargement of the breast. It is more common than the nodular variety. Retraction of the nipple has been reported in 2 cases. If the disease extends to the axillary glands, it pursues a much more rapid course than in the mammary gland. Occasionally the tuberculous process leads to the formation of a cold abscess, but this is rare, and never occurs before puberty.

SYMPTOMS.—The symptoms of tuberculous mastitis are pain and

tumor. The tumor may consist of one or more nodules, firm, hard, and freely movable with the gland. The skin may be freely movable over the growth, but frequently is attached. The nipple may or may not be retracted, and occasionally the entire breast becomes involved in one large, nodular, unyielding, brawny mass. The diagnosis is usually difficult, and is most important when the differentiation between tuberculosis and carcinoma is imperative. Under certain conditions it is impossible to distinguish them clinically. The infallible means of differentiation are the microscope and bacteriological culture. The axillary lymphatics are enlarged in three-fourths of all secondary cases; in other instances axillary involvement may be apparently absent; occasionally cervical glands are also infected.

ETIOLOGY.—Of the cases of tuberculosis of the mammary gland, 89.6 per cent. occur in females. The disease is most common between the ages of 20 and 35. Mammary tuberculosis may be primary, depending on infection through the milk-ducts or fissured nipples, or secondary, the disease extending from contagious foci in the chest, but extension from surrounding structures is the commoner method.

TREATMENT.—The treatment of primary mammary tuberculosis consists in **complete removal of the breast and axillary glands**. In the rare cases of *cold abscesses* these may be **aspirated** and **iodoform emulsion** injected.

The entire breast, as well as the axillary glands of the diseased side, should be removed. Only in a few cases, where single circumscribed nodules are present, may a partial

extirpation be done. In 10 of the writer's cases a complete **amputation** was done, the patients being able to go home in eight to fourteen days. E. Braendle (Beiträge z. klin. Chir., Bd. 1; Surg., Gynec., and Obstet., Dec., 1906).

While **excision of the breast** and **cleansing of the axilla** is the treatment of choice in a large number of cases of tuberculosis of the breast, there are also cases with superficial and subcutaneous localization, but no lymphatic reaction, in which evacuation by **aspiration** and injection of a modifying fluid, or else cauterization with the **thermocautery**, ought to be used, before taking up the more radical operation of excision of the breast. St. Jacques (Med. Rec., Feb. 27, 1909).

Operative treatment almost promises permanent cure in primary cases. In secondary forms prognosis depends entirely upon activity, location, and extent of the primary focus. In future the writer would advise **excision** of a tuberculous mass in the breast of a young woman, with exploration of the axilla for palpable lymph-nodes. In older women simple **amputation, with excision of axillary nodes**, is the best method. **Tuberculin** should be given, as it may perhaps aid nature in overcoming any small focus which might escape the knife. Conservatism is expressed rather in limiting the excision than in discarding operation. J. B. Deaver (Amer. Jour. Med. Sci., Feb., 1914).

SYPHILITIC TUMORS.

Gummata of the breast are not, according to Bissell, as rare as the authorities would lead us to infer, and such late syphilitic lesions can be quite easily differentiated by careful diagnosis. Many breasts sacrificed in the belief that they were cancerous could have been saved by the proper diagnosis. In case of doubt an attempt should be made by the quick

method of treatment to exclude absolutely the possibility of the tumor being syphilitic.

Gummatous tumors develop slowly and painlessly; they ulcerate and discharge much earlier than cancerous nodules; they are free from nodules early in their course; the nipple, as a rule, is not retracted, and the lymph-glands near may not be enlarged.

TREATMENT.—The best treatment is by means of **injection of the arseniosalicylate of mercury**, $\frac{1}{4}$ grain (0.016 Gm.) of which is given every third day until the tumor begins to disappear, combined, if it be needful, with the internal administration of **iodide of potassium**.

LACTATION, DISORDERS OF.

AGALACTIA.—Absence of the mammary secretion after parturition. The term is generally understood as meaning defective lactation, especially as to quantity.

Symptoms.—Absence of the mammary secretion after labor is rarely observed. The appearance of milk may be delayed days and even weeks, but evidence of functional activity usually appears, although frequently the quantity secreted is insufficient or the quality of the milk is not of a character to afford sufficient or proper nourishment to the infant.

Deficiency of secretion may occur from the start and continue throughout the entire period of lactation, or it may be normal in amount at first and gradually diminish.

Etiology.—Heredity is a prominent factor in case of true agalactia. Puech has reported the case of a woman who had given birth to 13 children, but whose breasts, though normal, had never yielded milk. Her

mother, who had given birth to 23 children, had likewise been absolutely sterile as regards the secretion of milk.

General ill health in which anemia plays the leading rôle is the most frequent cause of retarded, defective, or imperfect lactation. Lack of confidence, on the part of the mother, of her ability to nurse; excitement, fatigue, highly spiced food, overfeeding, and insufficient sleep may be mentioned as the most frequent auxiliary factors.

Injudicious dressing whereby the mammaræ are compressed, the pressure interfering with their circulation and proper nutrition, is a frequent cause of deficient lactation. Advanced age, especially in women who have suffered frequently from miscarriages, may also be included among the etiological factors. The habit of weaning early or avoiding lactation tends to cause atrophy of the breasts and to repress the lacteal secretion.

Prolonged suckling, specific affections, and iodide of potassium are also considered as causes of mammary atrophy, and, therefore, of deficient lactation.

Intercurrent affections, especially when acute, frequently arrest the flow of milk. High fever, when temporary, usually causes diminution of the secretion for the time being, and it may act as the primary factor of gradual cessation.

Pathology.—When there is total absence of mammary secretion, both breasts are usually affected. When the secretion is only defective, the involvement of the glands in the pathogenic process, local or general, is usually unequal, one mamma being less productive than the other. Large

breasts, owing to the quantity of adipose tissue present, are more likely to be agalactic than the smaller and thinner ones. The ducts and glands are usually found deficient in number and size, while the adipose tissue or the fibrous stroma is unduly abundant.

Treatment.—The first indication is carefully to inquire into the cause of the condition. In the majority of cases there is general deficiency in the performance of metabolic processes, due to general physical apathy. The patient should, therefore, be provided with **nutritious food** and appropriate tonics, especially **strychnin** and **hypophysis sicca**, both of which are peculiarly effective in these cases.

The bowels should be regulated by proper **dieting** and **massage** or **exercise** rather than by laxatives, and it is highly desirable that there should be at night uninterrupted sleep for six hours for mother and child.

Galactagogues are valueless in the majority of cases, most of them exerting practically no influence upon the gland. Occasionally a slight stimulating effect may be noted, but this lasts only a short time, and the organ soon lapses into its former torpor.

Beer, ale, porter, and other malt liquors, especially alcoholic beverages, are more hurtful than beneficial, and what improvement may show itself is due mainly to the confidence in the beverage taken, through the agency of autosuggestion. The quantity of milk may be increased, but its quality is compromised, especially when poor beer is consumed by the mother. It encourages the production of fat at the expense of the casein or milk-sugar. **Pure malt** may be substituted with great advantage.

Probably the most satisfactory among the galactagogues is *jaborandi*. The fluidextract or the tincture may be given in $\frac{1}{2}$ -fluidram (2 c.c.) doses. The active perspiration and salivation produced are objectionable, however, while the effects of the remedy are not lasting.

Castor-oil leaves have always borne considerable reputation. A **decoction** is made by boiling well a handful of them in 3 to 4 quarts of pure water. The breasts are bathed with this decoction for fifteen to twenty minutes. Part of the boiled leaves is then thinly spread over the breast and allowed to remain until all moisture has been removed from them by evaporation, and probably, in some measure, by absorption. The procedure is repeated at short intervals until the milk flows upon suction by the child, which it usually does in the course of a few hours (Routh).

Galega is credited with galactagogue properties, $\frac{1}{2}$ to 1 dram (2 to 4 Gm.) of the dried leaves or, better, the aqueous extract being given daily.

In cases of recent delivery in which the supply of milk is quickly diminished, the writer injects 1 c.c. (16 minims) of the **mother's own milk** subcutaneously, under strict asepsis. This is repeated in 2 days, and, if necessary, in 5 days again. Results are certain. C. H. Duncan (N. Y. Med. Jour., Jan. 6, 1917).

Small doses of **sucrose** or **dextrose**, such as 1 Gm. (15 grains) per 45 kilos. of body weight, regularly increased mammary secretion in a few hours. Sammartino (Arch. di farm. sper., Feb. 1, 1921).

Artificial suction with the **breast-pump** and **massage** are very commonly used. **Thyroid gland** is often helpful. Van Hoosen has employed **placental hormone**.

As to the **diet**, it should be as generous as the patient can digest. There is little to be gained by the common practice of prescribing 2 or 3 extra meals a day. A little broth or a glass of malted milk or plain milk between meals and at bedtime, however, is advantageous. The milk supply as well as the general health of the woman will depend more upon what she digests and assimilates than upon the amount of food taken into the stomach. Three daily meals, with, at most, the additional liquid stated, will generally be better than 5 or 6 meals. The difficulty in digesting milk, of which many patients complain, is, for the most part, imaginary. If taken as a part of the meal and not in addition to it, it will, as a rule, be well borne. Frequently patients who cannot use cold milk can take it hot without difficulty.

The secretion of milk is said to be greatly diminished by fatty food. A vegetable diet reduces the proportion of butter and casein and diminishes the sugar. A meat diet has the opposite effect. Systematic nursing with strict observance of stated intervals is essential for its influence upon both the quantity and quality of the milk secretion (Charles Jewett). Lobster, when available, is probably one of the greatest milk producers in the dietary.

POLYGALACTIA.—Polygalactia, or excessive secretion of milk, cannot be considered a pathological condition, except when it is exhausting the strength of the patient or when the profuse production of milk continues long after lactation has been suspended. The normal production in health approximates 3 pints in the twenty-four hours. Instances have been reported in which as much

as 7 quarts were secreted daily (de Mussy). It is evident that such a degree of hypersecretion need not be reached before emaciation, anemia, and even hectic symptoms appear. This is especially apt to be the case when loss of appetite attends the condition—not an unusual feature.

Treatment.—The active production of milk should be as much as possible arrested, but not too suddenly. In mild cases **suckling** should be **gradually abandoned**, the infant being increasingly nourished with artificial foods, and **tonics** be administered to the patient. In the meantime the breasts should be moderately compressed with a **breast binder**. Moderate compression in many instances is all that is required, together with **restriction in the amount of liquids consumed**.

As soon as the child can be weaned, **iodide of potassium** can be employed in increasing doses, beginning with such amounts as 5 grains (0.3 Gm.) three times a day.

The applications of a **belladonna plaster** or a weak solution of **atropine**—also **camphorated oil**—tend to reduce the excessive secretion, but there is always the danger of causing its cessation, so that the better plan is to **compress the breasts** moderately and administer in moderate doses internally **Rochelle salts**.

When the accumulation of milk cannot be sufficiently curtailed, the breast should be firmly compressed, withdrawing milk only when absolutely necessary.

GALACTORRHEA.—The continuance of milk secretion, with constant flow between the nursing periods, is usually the result of poor health and requires removal of the cause with

tonics, etc., and local measures such as are recommended for polygalactia.

A woman whose child had been breast-fed for 2 months complained of a discharge of milk from both breasts which had continued for over 2 years. **X-ray** treatment at once relieved the local pain and arrested the flow. Cameron, Ferrier and Thorlakson (Canad. Med. Assoc. Jour., June, 1924).

JOHN C. APPLIGATE,
Philadelphia.

MANGANESE.—Manganese (manganum) in the metallic state is not used in medicine.

PREPARATIONS AND DOSE.—There is but 1 official preparation of manganese.

Potassii permanganas, U. S. P. (potassium permanganate) [KMnO_4], occurs in dark-purple, slender, opaque prisms, and has a blue, metallic reflection, and a sweet taste, with astringent after-taste, soluble in 13.5 parts of cold and in 3.5 parts of boiling water. It is incompatible with all oxidizable substances, particularly organic ones. For pills it should be triturated with kaolin and massed with petrolatum. With glycerin permanganate solutions form a violent explosive. Dose, 1 to 2 grains (0.06 to 0.13 Gm.) in pill form.

Formerly official was:—

Mangani dioxidum præcipitatum, U. S. P. IX (precipitated dioxide of manganese; black oxide of manganese), containing chiefly manganese dioxide [MnO_2] with small amounts of other manganese oxides, and occurring as a heavy, black, fine, odorless powder, insoluble in water or alcohol, but soluble in hot mineral acids. Dose, 3 to 10 grains (0.2 to 0.6 Gm.).

The following are semi-official:—

Mangani citras solubilis, N. F. (soluble manganese citrate), occurs as a yellowish or pinkish white powder or translucent scales, with a slightly bitter and astringent taste, slowly soluble in 4 parts of water. Dose, 1 to 5 grains (0.06 to 0.3 Gm.).

Mangani glycerophosphas solubilis, N. F. (soluble manganese glycerophosphate), occurs as a yellowish or pinkish white powder, with an acid taste, soluble in 4 parts of water. Dose, 1 to 5 grains (0.06 to 0.3 Gm.).

Mangani hypophosphis, N. F. (manganese hypophosphite) $[\text{Mn}(\text{PH}_2\text{O}_2)_2 + \text{H}_2\text{O}]$, occurs as a pink, crystalline powder, soluble in 6.6 parts of water. Dose, 1 to 5 grains (0.06 to 0.3 Gm.).

Syrupus hypophosphitum compositus, N. F. (compound syrup of hypophosphites), contains $\frac{1}{8}$ grain (0.008 Gm.) of manganese hypophosphite per fluidram. Dose, 1 to 4 fluidrams (4 to 16 c.c.).

Liquor ferri peptonati et mangani, N. F. (solution of peptonized iron and manganese), an agreeably flavored, non-styptic solution, represents about 0.4 per cent. of metallic iron and 0.4 per cent of manganese in the form of soluble manganese citrate. The preparation contains about 15 per cent. of alcohol. Dose, 1 to 4 fluidrams (4 to 16 c.c.).

PHYSIOLOGICAL ACTION.—Manganese salts are absorbed from the alimentary tract only in small amounts—insufficiently to cause acute general toxic symptoms even after large doses. Injected hypodermically in animals, however, they produce distinct nervous and circulatory effects. According to Laschkewitz, the organic salts of manganese in moderate doses, given subcutaneously, slow the heart rate, lower the blood-pressure, and induce paralytic phenomena. After death from manganese poisoning the heart was found dilated and did not respond to electrical stimulation. In a case of acute poisoning in the human being, however, Phillips found the heart arrested in systole. Kobert observed that intravenous injection of manganese salts first transiently stimulated the vasomotor center, then paralyzed it; later, the heart itself was depressed and finally paralyzed. The cardiac nervous mechanism suffered first, and later the muscle. After massive toxic doses of manganese compounds, death is preceded by epileptiform convulsions.

Manganese, like iron, is eliminated mainly by the intestinal epithelium, and in less amount by the kidneys.

POISONING.

ACUTE MANGANESE POISONING.

—In excessive doses manganese causes gastroenteric inflammation, hemorrhagic nephritis with bile and albumin in the urine (but no manganese), and death.

CHRONIC MANGANESE POISONING.

—Emden reported 5 cases of poisoning among workers in manganese, through inhalation of the dust, and von Jaksch recorded 3 similar cases, in which the symptoms were irrepressible laughing and crying spells, muscular weakness and tremor of the lower extremities, exaggerated patellar reflex, a peculiar spastic gait, changed facial expression, and scanning speech.

Treatment of Poisoning.—Von Jaksch recommends **hydrotherapy**, **galvanization**, **faradization**, **exercise**, and the use of the **high-frequency current**.

THERAPEUTICS.—Manganese dioxide has at times proven useful in functional **amenorrhea**, especially when due to exposure to cold, and in **membranous dysmenorrhea**, in doses of 2 grains (0.12 Gm.), given in pill or capsule, four or five times daily. A. H. Smith found the **vertical headache** of cases of **dysmenorrhea** relieved by two or three doses.

In **anemia** and **chlorosis** manganese is considered by many beneficial, especially when combined with iron, as in the solution of iron peptonate with manganese (N. F.), given in the dose of a dessertspoonful or tablespoonful three or four times a day, either alone or in milk.

In **scrofula** and debility due to **chronic suppurative disease** the syrup of the iodides of iron and manganese (N. F.) is considered useful.

In **gastralgia** and **pyrosis** administration of the dioxide in doses of 10 grains (0.65 Gm.) has been recommended by Leared.

Potassium permanganate may be used with advantage as an antidote in **morphine**, **phosphorus**, and **snake-bite poisoning**. In 1884 B. Smith demonstrated its efficiency in morphine poisoning by taking 5 grains (0.3 Gm.) of morphine sulphate and a few seconds afterward 8 grains (0.5 Gm.) of potassium permanganate without suffering any narcotic effect. An equal quantity, grain for grain, of permanganate is antidotal. In cases of poisoning by opium (including laudanum) or the uncombined alkaloid morphine, acidulation of the antidotal solution with dilute sulphuric acid or white wine vinegar is advised, in order that the insoluble mor-

phine may be converted into a soluble salt.

In **phosphorus poisoning** the permanganate is a fairly dependable antidote. After washing out the stomach a pint (500 c.c.) of a 0.1 per cent. solution should be introduced and allowed to remain (Hagnos).

In **snake-bite poisoning** 20 minims (1.25 c.c.) of a 2 per cent. solution, freshly prepared, should be injected subcutaneously in 2 or more places, and especially into the orifices made by the fangs. It is a chemical, not a physiological, antidote, and does not preclude the use of antivenin.

Externally, potassium permanganate in solutions of 2 to 10 grains (0.12 to 0.6 Gm.) to the ounce (30 c.c.) of water is valuable as a deodorizer and disinfectant for **sloughing wounds, cancerous growths, ulcers, gangrenous areas, ozena, bromidrosis**, etc. In a 2 to 5 per cent. solution its use is advised in **leucorrhoea**, and in a 1 to 2 per cent. solution as an injection in **gonococcal urethritis**. In conditions causing a foul breath dilute permanganate solutions may be used as a mouth wash or spray.

Popoff found a 1:2000 permanganate solution useful for relieving rebellious **toothache** due to dental caries. One tablespoonful was taken into the mouth every half-hour, and held on the affected side for several minutes. W. M. Barton similarly points out that 1:2500 or 1:5000 solutions, used in irrigations of the urethra, produced anesthesia of the mucous membrane of this canal; this procedure is used by him to reduce local sensitiveness prior to the passage of sounds in cases of **urethral stricture**.

W. and S.

MANIA. See **PSYCHOSES**.

MASTITIS. See **MAMMARY GLAND**.

MASTOID PROCESS, DISEASES AND SURGERY OF. See **MIDDLE EAR, DISEASES OF**.

MEASLES. — DEFINITION.—Measles—morbilli or rubeola—is an acute, infectious, contagious disease generally met with in children.

SYMPTOMS.—Measles runs a less variable course, as a rule, than does scarlet fever and some other infectious diseases. Very mild cases sometimes occur, however, while the disease occasionally runs a very severe course. In rare instances a malignant type is encountered. Among 115 cases Carr found the average duration of the disease when uncomplicated to be twenty-six days from the prodromal symptoms to the end of desquamation. The period of incubation of measles is about twelve days.

Measles usually begins gradually with feverishness, sneezing, coryza, suffusion of the eyes, and photophobia. Occasionally a chill followed by a high temperature is the initial symptom. Within twenty-four hours after the advent of the first symptoms a cough of peculiarly hard, dry character appears and the attack presents all the symptoms of a catarrhal cold. The coryza, however, is more marked than that of an ordinary cold. The fever often falls somewhat after the first day, a fact which may throw the physician off his guard. The coryza and cough, however, do not correspondingly diminish with the fall of the temperature, but usually increase. The eruption appears on the side of the face and is usually first seen on the afternoon of the fourth day and is accompanied by increased fever. The eruption may appear as early as the second day, particularly in young children, and is, in rare instances, delayed to the fifth or sixth day. Drowsiness is not uncommon during the stages of invasion, but there are no characteristic constitutional symptoms.

A distinct loss of weight has been observed by some authorities on the fourth and fifth days after exposure.

This is known as Meunier's sign. As described by that observer, it consists of a progressive loss of weight of about $1\frac{1}{2}$ ounces each day from the fourth day of the exposure to the onset of symptoms.

Koplik has described a symptom which he believes to be of great value in making an early diagnosis of measles. On the first day of invasion he has found that an examination of the buccal mucous membrane in a good light will reveal a scattered eruption consisting of small, irregular spots of bright-red color in the center of each of which is a minute, bluish-white speck. This he regarded as pathognomonic of measles. Most authorities put much reliance upon this symptom. The spots are most abundant along the line of the molar teeth.

Koplik's spots do not invariably accompany or precede measles, but the writer always found in cases which proved to be measles peculiar whitish efflorescences on the tonsils, punctate or linear, about 3 mm. long. This is a reliable sign and the earliest one of oncoming measles. Grumann (Münch. med. Woch., Jan. 20, 1914).

In 3 children with measles the writer observed Koplik's spots on the nasal mucous membrane. Steinert (Med. Klin., June 5, 1925).

The temperature will occasionally be found at 103° or 104° on the first day, but it is usually not above 102° . The fever does not ordinarily range as high in measles as in scarlet fever. Not infrequently after a sharp rise on the first day the temperature falls on the two following days, but increases as the eruption appears and reaches its height on the second day of the eruption. From that time it gradually falls, and becomes normal between the seventh and ninth days of the disease. Not infrequently there is a sudden fall on the

sixth or seventh day, forming almost a crisis. The fall of the temperature after the initial rise on the first day is sometimes so decided as to lead to error in diagnosis. The possibility of such a fall is always to be considered. The fever and other constitutional symptoms are usually at their height when the eruption has reached its fullest development on the fifth or sixth day of the disease.

The rash usually appears on the afternoon of the fourth day, but in some cases is seen on the third day and in others is delayed until the fifth day. It is first seen on the temples and sides of the face, on the neck, or behind the ears. When it first appears it commonly consists of small red spots having no strictly characteristic appearance. They rapidly increase in size and form small macules or very slightly elevated papules on a slightly reddened base with normal skin between. They are circular or crescentic in shape, and, being hyperemic in nature, disappear on pressure.

As the eruption develops it tends to become confluent in places, particularly on the face, where it assumes a blotched appearance. There is usually a certain amount of edema, particularly about the cheeks and eyes, which farther tends to change the appearance of the patient. The eruption usually reaches its height at its first site of appearance at the end of thirty-six hours; it remains stationary for about two days, and then rapidly fades away. It extends over the body somewhat slowly, appearing on the trunk and limbs on the second day.

The wrists and backs of the hands are commonly the points to be last involved. When at its height in these places, the rash is sometimes partially faded on the face and neck. On the first day the

spots form simple macules, but later they become flat papules that can be readily felt by the fingers and are sometimes almost shotty to the touch. The rash commonly presents its most typical appearance on the chest.

The typical rash of measles is frequently accompanied by miliary vesicles and in rare cases petechiæ appear. Occasionally the rash, instead of assuming the usual hyperemic form, becomes distinctly hemorrhagic. This may occur in limited areas or may extend over the whole body. In the latter case it presents the type known as "black measles," a condition extremely rare in private practice. It indicates a severe form of the disease, but is not generally fatal, as is popularly supposed. The spread of the eruption is sometimes extremely rapid, the whole body being covered in a few hours, but this is rare. In other rare instances the rash is so slight and of such short duration as to be almost overlooked. The constitutional symptoms in such cases are, as a rule, correspondingly mild. Occasionally in malignant cases, marked by sudden or severe initial symptoms, the rash scarcely appears or is much delayed.

The constitutional symptoms reach their height during the stage of eruption, being usually at a maximum on the sixth day of the disease. They then remain stationary for about two days, when the fever abates and all the symptoms begin to subside. This sometimes occurs so suddenly on the sixth or seventh day as to form a crisis. This, however, is not the rule.

Albuminuria is not infrequent in the febrile stage, but nephritis is rare. The diazo reaction is found in about 80 per cent. of the cases.

There is an early modification in the blood-picture, consisting of a de-

crease of the lymphocytes and relative increase of the polynuclears, together with a general leukopenia. The normal 50 to 70 per cent. of lymphocytes and 25 to 35 per cent. of polynuclears in infants may thus be actually reversed. This condition, occurring in the period of incubation, is an early diagnostic sign in suspected cases. The leukopenia is stated to persist through the course of the disease. A leukocytosis appearing late in the course of measles points to a complication.

In 14 children whose blood was examined during the incubation period of measles, Hecker noted the pronounced reduction of the white corpuscles fully $4\frac{1}{2}$ days before the eruption and $3\frac{1}{2}$ days before Koplik's spots were manifest. Two or three days before the eruption, however, the leukocyte count was increased.

Bleyer has brought out the fact that enlargement of the spleen may be included in the symptomatology of measles. The spleen, in many cases, enlarges rather abruptly during the eruptive stage and subsides suddenly with the disappearance of the rash.

Of 47 cases examined on the day before the eruption appeared, only 2 per cent. showed enlarged spleen. Of 58 examined on the first day of the rash, 24 per cent. had enlarged spleen, and of 80 examined on the second day, 43 per cent. Of 62 examined on the third day of the rash 56 per cent. had enlarged spleen, and of 49 examined on the fourth day, 52 per cent. Thus, the splenic enlargement was coincidental with the eruptive stage. The severity of the attack did not appear to affect the incidence of enlarged spleen. A. Bleyer (*Amer. Jour. Dis. of Childr.*, Jan., 1926).

During the height of the disease the patient presents a very characteristic appearance. The face is covered by a

patchy eruption and is swelled and edematous; the eyes are red and sensitive to the light and are filled with a mucus or mucopurulent secretion; the nose is swelled and discharges a similar secretion; there is a dry, metallic, and very troublesome cough; the tongue is coated; the appetite is completely lost; the bowels are frequently relaxed; the child lies in a heavy and stupid condition, but is restless and irritable when disturbed. The glands at the angle of the jaw are often enlarged, and not infrequently the postcervical glands, also.

As the fever subsides, the cough rapidly changes its character, becoming looser and less irritating. It frequently disappears within a week, but sometimes the evidences of bronchitis continue, and the cough proves a troublesome symptom for several weeks. In most cases the photophobia subsides rapidly, but the eyes are prone to remain weak and watery. If strong light is admitted too soon a mild but very troublesome and persistent form of conjunctivitis may result. Other symptoms usually subside rapidly; the child becomes brighter and less irritable; the appetite returns, and evidences of illness soon disappear.

Desquamation begins as soon as the eruption has faded, and follows the order of its appearance. It rarely continues more than ten days in any given area, and may be of much shorter duration. It is most intense where the eruption has been most intense. It occurs in fine, branny scales quite unlike the lamellar desquamation of scarlet fever. It is often so slight as to be completely overlooked, particularly when inunctions of the skin have been carefully used. Desquamation is usually completed in from twenty to twenty-four days after the onset of the disease.

IRREGULAR FORMS.—Measles is capable of assuming very irregular and atypical forms. Such irregular types are most common in children under 3 years. Nevertheless, in a given number of cases a much larger proportion of measles cases will run a typical course than will a similar number of cases of scarlet fever.

Mild Type.—The disease may be extremely mild, the eruption being faint, the fever slight, and all the symptoms mild. Such cases present no variation from the usual type except that of mildness in degree. Although the catarrhal symptoms may be slight, the diagnosis of *morbilli sine catarrho* should be made with extreme hesitation.

Severe Type.—A severe form is sometimes seen, marked by unusually high temperature, intense eruption, and severity of all the symptoms. Except in young children, the uncomplicated disease, even when of severe type, is rarely fatal. But it should not be forgotten that a temperature that reaches an unusually high point or continues unabated as the eruption fades is usually due to some complication, commonly pulmonary. Any marked variation from the usual type demands particular attention, for it commonly indicates a complication.

Malignant Type.—Malignant measles, marked by intense and overwhelming symptoms from the outset, is fortunately rare outside of institutions. The same is true of hemorrhagic, or black, measles.

Relapse in measles is extremely rare and is, in fact, of doubtful occurrence. A secondary rise in temperature after a normal fall indicates a complication.

ETIOLOGY.—Measles is doubtless due to bacterial action, but no specific micro-organism has yet been positively identified, although the green-producing streptococci isolated by Tunncliffe and by Ferry and Fisher have attracted much attention, and in Italy the discovery of a specific organism has been credited to Caronia.

The vitality of the agent of measles would appear to be small, though it must be extremely diffusible, for measles is the most contagious of the infectious diseases, except small-pox.

The writer has described Gram-positive diplococci which she isolated in anaerobic cultures from the blood of measles and rubella patients. The diplococcus of measles is small and round, while that of rubella is larger, has pointed ends, and is elongated and encapsulated. From a study of smears taken from the most highly inflamed areas of the throats of patients having measles, rubella or scarlet fever, and from normal persons, the features of the smears were found to be of decided diagnostic value. In measles there were generally some polynuclear and epithelial cells and many of the small, round diplococci. R. Tunncliffe (Jour. Amer. Med. Assoc., July 13, 1918).

Report of the isolation in pure culture of an organism—*Streptococcus morbilli*—from the blood of early measles cases, as well as the preparation from it of a measles toxin and the application of the latter as a skin test, as an immunizing agent, and for the production of an antitoxin.

The germ is a small, Gram-positive, aerobic, green-producing streptococcus, appearing in pairs and chains. Proof of the specificity of the germ and its toxin was obtained by experiments on persons susceptible to, immune to, or suffering from measles, as well as on rabbits and other animals. Of 35 persons without a history of measles, 14 gave positive skin reactions

on intracutaneous injections of 0.1 c.c. of a 1:500 dilution of the toxin; the technic was similar to that for the Schick or Dick test, and a reaction 1 cm. or more in diameter was considered positive. Of 30 children with a history of measles none gave a positive skin test. Patients in the eruptive and early stages of the disease gave positive skin reactions, while those in the later stages, and especially convalescents, gave negative reactions. When mixed with measles convalescent serum or with serum from an animal immunized with the toxin, the toxin will not produce a positive skin reaction in susceptible persons. Persons giving positive skin reactions are made to give negative reactions by subcutaneous injections of measles convalescent serum. Serum of measles convalescents agglutinates suspensions of the measles streptococcus, while negative serum does not. N. S. Ferry and L. W. Fisher (Jour. Amer. Med. Assoc., Mar. 27, 1926).

Its occurrence is uncommon under six months, but above that age every child who has not already had it may be expected to contract it upon exposure.

Adults are rather more susceptible to it than to the other infectious diseases. Measles is endemic in all large towns, but at intervals it becomes epidemic and spreads over a wide area before it expends itself. Sex is not a predisposing factor.

Where the disease is introduced for the first time it attacks adults and is often fatal. In 1875, in the Fiji Islands, as many as 40,000 of the 150,000 inhabitants died of measles (O'Meara).

In 1000 cases of measles studied, the most common causes of death were bronchopneumonia and enteritis: 23.3 per cent. of total deaths. Average duration of the fever, four days. The onset of purulent otitis media on the tenth or twelfth day

may not be attended by unusual fever. If the temperature remains high after the fourth day, a possible complication is imminent. Craster (Am. Jour. Dis. of Child., Aug., 1913).

Sources of Infection.—Measles is transmitted by direct contact, but the area of contagion is large. Although intermediate contagion may occur, it is comparatively rare. The infectious power of the poison is quickly lost, so that sick-rooms very soon become safe for occupancy.

It is probable that contagium may be conveyed by the breath; but it is certain that it resides in the sputa and the discharges from the nose and eyes. Ample experimental evidence has shown, however, that infection is not carried through the air for a distance greater than 9 feet.

If the contagion resides in the desquamation scales, it is far less potent than is the poison carried by the desquamation of scarlet fever. The disease may be conveyed by clothing or it may be contracted by a susceptible person entering a room recently left by a measles patient.

Seventeen specimens of measles sputum were examined by the writer on the first or second day after the appearance of the eruption. Direct smears of the washed sputum showed small (0.5 microns) round or very slightly elongated Gram-positive diplococci. The diplococcus was isolated from all of the sputum examined. *B. influenza* and *S. hemolyticus* were each isolated twice. Ruth Tunnicliffe (Jour. of Infect. Dis., Feb., 1919).

Incubation.—The period of incubation ranges from nine to twenty-one days. Holt found it to be between eleven and fourteen days in 66 per cent. of 144 carefully observed cases. I have repeatedly seen the initial symptoms appear 12 days after ex-

posure which corresponds with the evidence available in literature.

The writer observed 2 typical attacks of measles in his own child with an interval of 3 years, and collected records of 46 families. There had been 71 cases of measles in which the incubation period could be determined with precision: 10 days in 15 cases; 9 in 12; 11 in 12; 8 in 10; 7 in 5; 12 in 5; 13 in 5; 6 in 2; and from 14 to 19 in 1 case each. Lewy Zeit. f. Kinderheilk., Aug. 16, 1920).

Transmission.—Measles may be contagious from the first appearance of the catarrhal symptoms, authentic cases being recorded in which the disease was transmitted four days before the eruption appeared. It is most contagious during the height of the catarrhal stage and until the eruption has reached its climax. The contagiousness diminishes as the active symptoms subside, and is slight during the stage of desquamation. Except in complicated cases, in which the catarrhal symptoms are usually prolonged, the period of infection is not over twenty-eight days.

The writers succeeded in infecting a monkey of the species *Macacus sinicus* with measles by injecting intraperitoneally 6 c.c. of the blood of a child suffering from the preliminary symptoms of the disease. This shows conclusively that measles is contagious before the eruptive stage. C. Nicolle and E. Conseil (Acad. de Méd.; Bull. méd., Jan. 3, 1912).

The writers produced measles in monkeys by inoculation of blood-serum from a patient thirty-six hours after the initial rise of temperature and six hours before the appearance of the rash. The monkeys, after a definite incubation period of six days in 1 case, showed systemic signs, and on the tenth day Koplik spots could be seen. Lucas and Prizer (Jour. of Med. Research, Apr., 1912).

Monkeys which recovered from experimental measles were found immune to reinfection with the virus, whether the latter was of homologous or heterologous origin. This corresponds with measles in human beings, whether the virus is inoculated on the respiratory mucosa or is injected intravenously. Blake and Trask (Jour. Exper. Med., May, 1921).

PATHOLOGY.—In uncomplicated measles the lesions are confined to the skin and the mucous membranes of the conjunctivæ, nose, pharynx, larynx, and the larger bronchial tubes. The morbid changes of the skin are those of acute hyperemia; on the mucous membranes they are those of acute catarrh. In complicated cases pseudomembranous inflammation may occur. Death rarely results from the simple disease, but rather from the complications, which will be considered later. The complications are due to mixed infection, a germ commonly present being the staphylococcus. A streptococcus is, however, frequently to be found, and, as a rule, causes more serious lesions than those due to the staphylococcus. The mucous membranes are rendered very susceptible by measles to these germs. As they are invariably present in the wards of hospitals, the disease in such institutions is always a dreaded one, for it is prone to be complicated.

According to Von Pirquet, the eruption in measles is an antitoxic reaction to the organisms causing the disease, which are located in the capillaries. The organisms are agglutinated and the eruption appears when the capillaries of a given region become saturated with antibodies. This saturation takes place first in the regions having the most abundant blood-supply, such as the mucous membranes and the regions near the heart and large blood-vessels. Gradually the organisms are removed from

the circulation by agglutination. By the time the parts with a less abundant blood-supply, such as the elbows, feet, and nates, have developed a sufficient supply of antibodies, there are no longer any organisms to agglutinate; therefore, those parts show no eruption.

In 8 out of 11 fatal cases of measles examined *post mortem*, death had been due to bronchopneumonia. In 3 cases, however, death occurred so early—3, 18 and 24 hours after the appearance of the rash—that bronchopneumonia of any important extent had not developed; these 3 deaths are ascribed to uncomplicated measles, and the lesions found are considered the primary lesions of this disease. These lesions are located in the lower trachea, bronchi and contiguous lung. The mouth and pharynx showed: (a) Focal necroses of the epithelium, with subjacent reaction in the endothelium of the papillary vessels, and the later formation of small ulcers; (b) suppurative lesions in and about small submucous glands and their ducts; (c) inflammatory lesions of small submucous lymph follicles. The Koplik's spot is an inflammatory lesion of a submucous gland, and the bluish halo about it is due to the collar-like plexus of dilated venules about the duct. In the larynx and trachea the mucous membrane is edematous and groups of superficial cells and solitary deeper cells are undergoing degenerative and vacuolar changes. In the bronchi the lesions are similar, but complicated in places by rather extensive destruction of epithelium. A slight primary injury to the lung, bronchopneumonic in type, was also found. J. Denton (Amer. Jour. Med. Sci., Apr., 1925).

COMPLICATIONS AND SEQUELÆ.—The most common and serious complications of measles are bronchopneumonia, membranous laryngitis, and otitis; the most common sequelæ are tuberculosis and conjunctivitis.

Bronchial catarrh is an essential

part of measles, but it is very easy for the inflammation to extend from the smaller bronchi to the alveoli, thus transforming a normal condition into a most serious complication,—namely, **bronchopneumonia**. The younger the child, the greater is this danger. It occurs chiefly in children under 3 years, and is comparatively rare in children over 4 years. It is very common in institutions and renders measles the most dreaded of all epidemic diseases in infant hospitals, diphtheria being no exception to the rule. In an epidemic of measles in the Infants' Hospital of New York every case in children under 18 months was complicated by bronchopneumonia or **croup**, and 80 per cent. died. The pneumonia usually made its appearance soon after the eruption reached its height, but developed in a few cases during the stage of invasion, the disease being regarded in two instances as simple bronchopneumonia until the eruption suddenly appeared. Holt asserted that 10 per cent. of all cases are complicated by bronchopneumonia. He agreed with Hensch that a certain amount of pneumonia is found at autopsy in almost every fatal case. Carr found it clinically 21 times among 115 hospital patients.

Lobar pneumonia is an occasional complication of measles in children over 4 years, but is seldom if ever found under 3 years. **Empyema** is sometimes a sequel of such complicating lobar pneumonia. The signs and rational symptoms of either form of pneumonia complicating measles present nothing unusual.

Study of 437 cases of measles affording striking evidence of the fact that death in this affection de-

pends upon the pulmonary complications, such as bronchitis, pneumonia, and bronchopneumonia. In the first five years of life the curves of incidence of pulmonary complications and of death are parallel. The total death rate of the epidemic observed was 5.03 per cent. Severe pulmonary complications were present in 23.57 per cent. of all cases. Tait (Brit. Med. Jour., June 29, 1912).

In 388 cases in troops, broncho-pneumonia occurred in 47, or 12.1 per cent. Of these, 15 or 34 per cent. developed empyema. The pleural fluids showed *S. hemolyticus*. Levy (War Med., Paris, Nov., 1918).

Catarrhal pharyngitis is an essential part of measles; **pseudomembranous pharyngitis** sometimes occurs as a complication. Instead of invading the nose and ears, as in scarlet fever, it shows a strong tendency to invade the larynx; but **croup** frequently develops without the appearance of membrane in the pharynx.

As in scarlet fever, the pseudomembranes which develop during the height of the attack are usually due to streptococci, and are, therefore, not true diphtheria. Those which develop later are usually due to Klebs-Loeffler bacilli and are true **diphtheria**. This secondary streptococcic disease, however, is quite as fatal as the bacillary disease. Not only is the child in imminent danger from laryngeal complications, but it is almost certain, also, to develop bronchopneumonia, which occurs as the direct result of streptococcic infection. The differential diagnosis between true and false diphtheria can rarely be made with certainty from clinical appearances alone. Fortunately, in private practice both complications are rare in children over 4 years.

Otitis, while less common than in scarlet fever, sometimes occurs, but does not usually prove so serious. Both ears are usually involved, but the disease presents in its symptoms and course nothing worthy of particular mention.

Complete **anorexia** is common during the febrile stage. **Diarrhea** is of frequent occurrence, and occasionally is so severe as to prove a serious complication. It may be due to simple intestinal indigestion, or it may be the evidence of enterocolitis.

Febrile **albuminuria** is not infrequent in cases with high temperature, but **nephritis** is uncommon.

Nervous symptoms, excepting the occasional appearance of **convulsions** at the outset, are rare.

Licciardi reported the case of a child nearly 2 years old, who developed **spasm of the larynx** during the eruptive stage. The vocal cords seemed to contract slowly until the carbon dioxide accumulating in the blood stimulated the respiratory center and induced a profound inspiration. The spasm was then suspended for an instant. While considering intubation, mustard to the chest and bromides, cannabis and belladonna were given, and in a few hours the spasm subsided. It returned again 2 days later, when it yielded as before to the same measures. Another child had attacks of typical **asthma** for the first time during measles. In a third, the **spasm** affected the **intestines**; the intense pain, unaccompanied by any objective signs, continued unmitigated until relieved by bromides, cannabis and belladonna.

Case of **encephalitis** following measles in a girl of 13 years. Fever continued after apparent recovery from the measles and on the 20th day convulsions appeared. These soon became limited to the right side and were replaced by hemiplegia on that side, with aphasia. Subsequently there was slow improvement in this condition. Bonaba (*Arch. Lat.-Amer. de Ped.*, June, 1925).

Endocarditis and **pericarditis** are seen in rare cases.

Report of 2 cases showing **disturbances of local circulation** after measles. In one there was a waxy pallor and coldness of the feet, which in 2 days extended up to the umbilicus, ascribed by the writer to capillary spasm. Treatment was ineffective. In the other case there was paroxysmal cyanosis and edema of the extremities, attributed to toxic paralysis of the capillaries. This condition would yield temporarily to hot applications and massage, but returned upon discontinuance of the treatment. Ultimately, however, it passed off permanently. Händel (*Monat. f. Kind.*, Apr., 1925).

Meningitis may occur as a further complication, through the presence of otitis.

Cellulitis and **suppurative adenitis** are uncommon, but moderate **enlargement of cervical glands** often occurs and sometimes persists for months.

The occurrence of measles simultaneously with other infectious diseases is not very infrequent. There seems to be a particular tendency to the simultaneous occurrence of measles and **pertussis**.

Hutinel saw 5 cases of **scarlet fever** succeeding measles. All recovered without any complication. The gravity of the former disease in such cases depends on whether the measles is complicated or not by bronchopneumonia or bronchitis. If scarlet fever and measles coexist (a very rare condition), the eruptions are simultaneous, but this combination is not serious. The most serious condition is when measles follows scarlet fever. Out of 15 cases 4 died, all from pulmonary complications. The shorter the interval between the two fevers, the more grave the outlook.

Tuberculosis is the most serious sequel of measles. It commonly occurs as a tuberculous bronchopneumonia, general miliary tuberculosis, tuberculous adenitis, or tuberculous

joint disease. These conditions may result from primary infection or from the lighting up of some old tuberculous process. Measles unquestionably renders the tissue very susceptible to tubercle bacilli, so that infection may result from slight exposure. **Acute miliary tuberculosis** may follow measles at once, the temperature range being continuous from the outset of the primary disease to death from the complication. General tuberculosis with grave pulmonary involvement may follow so close upon measles as to leave no appreciable interval between. It is sometimes the cause of a secondary fever, which develops soon after the subsidence of the primary fever. Tuberculous disease of the bones and joints subsequent to measles is usually of late occurrence.

Chronic conjunctivitis is a frequent sequel of measles which may be in large degree prevented by judicious care. **Iritis** and **keratitis** are possible sequels, but are not common.

DIAGNOSIS.—Measles is distinguished from scarlet fever chiefly by the coryza and other catarrhal manifestations of the former, the absence of leucocytosis, and the presence of Koplik's spots. Sore throat, a diffuse eruption, and glandular enlargement are suggestive of scarlet fever, but at times prove unreliable diagnostic guides, being sometimes present to a moderate degree in measles.

Biehler, examining 947 cases for the Koplik spots, found them the day before the eruption in 864, two days before in 42, and ten days before in 1.

When dry cupping was applied to the chest or back for 30, 40 or 50 seconds, in 200 healthy persons there was left a whitish ring. When applied during the incubation stage of measles,

3 days before the eruption appeared, a reddish ring was seen. If applied 48 hours before the eruption, the red circle is much wider and the color deeper; 12 hours before the eruption the red circle is still wider and the color veers more to purple. This induced erythema reaches its height in $3\frac{1}{2}$ minutes and then subsides, lingering sometimes up to 10 minutes. The 18 who gave a positive reaction developed a typical measles eruption 4 or 5 days afterward. Godlewski (Bull. Soc. méd. des hôp. de Paris, Nov. 23, 1917).

According to Herrman, the earliest symptoms of measles appear at the following average times after exposure: Fever, 10 days and 11 hours; tonsillar spots, 11 days; catarrh, 11 days, 15 hours; Koplik's spots, 12 days, 2 hours; eruption, 13 days, 14 hours. The time varies widely in different cases, but the order of appearance is fairly constant. Koplik's spots can often be found on the caruncle at the inner canthus of the eye. According to Brownlee, the first symptom is fever, and the second, edema of the conjunctiva, especially that of the lower lid. In institutions the thermometer can thus detect secondary cases 24 hours before the catarrh. P. M. Stimson (Arch. of Ped., Jan., 1922).

From rubella or German measles (*q.v.*), rubeola is differentiated mainly through the slight or absent prodromata, the absence of Koplik's spots, and also through the earlier and more evanescent eruption in the former affection. The papules in rubella, which often appear as the first observable symptom, are more discrete than in measles. Fever is not so pronounced and complications do not occur.

In the differential diagnosis between scarlet fever, measles, and German measles, a clinical sign which often proves very helpful consists in free perspiration during the entire course of German measles, whereas

the skin is invariably dry and more or less hot in scarlatina and morbilli. The free perspiration is due to the fact that in German measles not only the lymphatic glands (including the spleen, which is often greatly enlarged), but the sudoriferous glands as well, are involved. Herman B. Sheffield (*Med. Rec.*, Aug. 9, 1913).

From small-pox and typhus, with which it has been at times confounded, measles is distinguished by the Koplik spots and, in general, by the less violent constitutional manifestations.

The prodromal conjunctivitis of measles presents special characters which distinguish it from that of ordinary coryza. In the latter the injection of the mucous membrane usually begins at the cul-de-sac of the eyelids, whence it extends to the ocular and palpebral surfaces. In the early conjunctivitis of measles the first sign of injection is observed on the bulbar conjunctiva on either side of the cornea directly opposite the palpebral fissure. If seen sufficiently early, the redness occupies the usual situation of pterygium, but it spreads so rapidly that by the following day the whole mucous membrane of the eye is involved. This sign was found in over 70 per cent. of the cases examined. A. Aly-Belfadel (*Semaine méd.*, Jan. 8, 1908).

Exanthemata very similar to that of measles occur, among other infections, in dengue, bilious typhoid, and Rocky Mountain fever. Goetz (*Jahrbuch. f. Kinderheilk.*, Aug., 1912).

PROGNOSIS.—Death from measles in private practice is rare in children over 4 years of age. Holt, after the study of a large number of cases, concluded that the mortality of the disease is from 4 to 6 per cent., but under 2 years it is often 20 per cent. or more. It is highest between 1 and 2 years, but even at this age uncomplicated measles is not a highly fatal

disease. Pneumonia is the cause of death in almost 90 per cent. of fatal cases.

A violent onset with high temperature warrants a guarded prognosis. A rising temperature with a fading eruption warrants an unfavorable prognosis. The same is true when the eruption is excessive in amount and confluent over wide areas. Grave general symptoms with faint eruption is a serious condition. The same is true of a hemorrhagic or black eruption, but it is not as necessarily fatal as is commonly supposed.

Measles has a marked tendency to leave behind it results of a serious nature. Treatment should not be directed solely to saving the life of the child nor should the prognosis be made up solely with reference to that event. The tendency to tuberculous invasion should never be forgotten, and when the fever persists after the tenth day, even if it is not high, the prognosis should be guarded. The list of chronic affections left in the wake of measles is a long one; bronchitis, pharyngitis, rhinitis, adenoid growths, enlarged tonsils and mesenteric glands are among the number which should receive consideration.

PROPHYLAXIS.—The advisability of taking particular precautions against the exposure of infants is suggested by the high mortality of measles before 3 years. Delicate children of the so-called scrofulous type and those with hereditary tendency to tuberculosis should be especially guarded against exposure. Early and absolute isolation of the sick is imperative. Quarantine of the patient should not be less than fourteen days and as much longer as purulent discharges may continue. Children

who have been exposed should be isolated from other children for at least that period, and twenty days is preferable. A non-immune exposed individual showing a rise of temperature of 0.5° C. (0.9° F.) or more should be promptly isolated pending diagnosis.

The sick-room after recovery of the patient is less liable to prove dangerous than is the scarlet-fever sick-room. Thorough **cleansing** and **ventilation** after the patient has left it are sufficient. The infection of measles is not persistent nor is intermediate infection common, so that prolonged precautions are not necessary. During the disease the same measures should be taken to **avoid the exposure of others** as in other infectious diseases.

Such measures as **gowns, caps, and personal disinfection of attendants** should always be adopted, but it is the consensus of opinion that they are of less value than in diphtheria and scarlet fever. **Absolute isolation of the patient and prevention of contact with non-immunes** should be enforced.

Raffle has emphasized, on the basis of a personal statistical study, the part played by the school in the spread of measles and the value of **school closure** in an epidemic as a preventive measure. Some advise, however, against school closure where daily observation of the children by a physician or nurse is provided for.

Experience confirms the fact that the **eucalyptus oil neck bag** is effectual in the prophylaxis of measles. Elgart (Med. Klinik, Aug. 3, 1913).

Prophylactic use of **convalescent serum**, first applied by Park and Zingher in 1916 in this country, and also in France in the same year by Nicolle and Conseil, is usually com-

pletely effective. Either serum, plasma or whole blood can be used.

The preventive injection is effective if given before the 6th day of incubation; otherwise it tends only to diminish the severity of the infection. The dose for infants is 2 c.c.; 4 or 6 c.c. for older children. It should be larger in the later stages of incubation. Méry, Gastinel and Joannon (Bull. de l'Acad. de méd., Feb. 6, 1923).

Having noticed that prophylactic injection of diphtheria antitoxin tended to prevent measles, the writer tried **normal horse serum**, at least 5 c.c. (80 minims). Out of 24 exposed children thus treated, only 1 developed measles. Galli (Pediatri, Oct. 1, 1922).

The writer used the **serum** only, obtained either from **convalescent** measles cases, recovered cases, or from **healthy adults** who had had measles at some time. Unmistakable measles cases were preferred, the blood being collected 5 to 10 days after the temperature was normal. Among 122 subjects treated, only 6 developed measles; 3 of these ran a typical course, the remaining 3 a modified form. All of 96 cases had been definitely exposed to measles; only 4 of them developed measles, after 22 to 28 days. The duration of the protection period is 40 days. Woody (Mo. Bull. Dept. of Publ. Health, Phila., Sept., 1924).

Serum of adults with a history of measles prevented the disease in 75 per cent. when used in the beginning of the incubation stage; 20 per cent. developed an attenuated measles, and 5 per cent., typical measles. The dose was 12 to 15 c.c. in infants not over 2 years and 20 to 25 c.c. above this age. Mixed serums from several persons are preferred, and likewise serum from parents. Serum from persons convalescent from other infectious diseases also proved efficient. Debré (Bull. Soc. méd. des hôp. de Paris, May 8, 1925).

Of 389 patients receiving 3 to 10 c.c. of **convalescent serum** intramuscularly, only 21 developed a mild measles, 13 before and 8 after the usual incubation

period of 14 days. The serum had been obtained 8 days after disappearance of the rash, and was inactivated 1 hour at 56° C., sealed and stored on ice, no preservative being added. Serum even 8 to 12 months old still seemed potent. Toomey (Amer. Jour. Dis. of Childr., Sept., 1926).

TREATMENT.—The patient should be placed in as **large and well ventilated** a room as possible. The temperature should not be kept at too high a point, nor should the child be forced to swelter under too heavy covering. It accomplishes no good and renders the child restless and irritable. It has been the custom to keep the **room dark** and **avoid direct light falling upon the eyes**. As the inflammation of the eyes subsides, the light should be gradually admitted, but full light should not be permitted until the conjunctivæ have become normal in appearance. Itching of the lids should be relieved by **cold cloths** or by the application of **cold cream** or some **bland oil**. The eyes should be kept clean by washing out once or twice daily with a solution of **boric acid**, or **normal saline solution**.

The child should be put to **bed**, even in the mildest cases, and kept there until desquamation is practically completed. The diet should consist of **milk** and **broth** during the febrile stage; during the height of the disease the child should not be over-urged to eat.

Initial administration of **calomel** followed by **castor oil** or a **saline** is probably of advantage.

The upper respiratory passages and pharynx should be cleansed by use at suitable intervals of a **spray** and **gargle** of some mild **alkaline** and **antiseptic solution** or **normal saline**.

Applications of plain or **carbolyzed petrolatum** do much to reduce the irritability of the skin. As soon as the eruption begins to subside, **unctions** of plain or carbolyzed petrolatum or **ichthyol ointment** should be practised daily. A **daily warm bath** does much to hasten desquamation.

The hard, metallic cough is one of the most troublesome symptoms of the disease. Very little relief, however, can be afforded by treatment before the fever begins to subside. It cannot be loosened by the administration of nauseating expectorants. They tend to render the child more irritable and to increase the anorexia and have but slight effect on the cough. Small doses of **opium** aid in allaying the cough, and are quite permissible. **Brown mixture** in the form of tablet triturates is as effective as any treatment and is easy of administration. Small doses of **codeine** are also serviceable.

For a croupy condition at the start of the disease **cold** or **hot compresses** are of value, and **inhalations** of **compound tincture of benzoin** with a croup kettle and tent may likewise be availed of. Where there is a tendency to laryngeal edema, a **spray** of 1:20,000 **adrenalin** may be tried.

Some practitioners use **quinine** internally, **hot lemonade** and **blankets** to bring out the eruption where it is scanty or delayed, on the ground that this is likely to forestall serious illness or complications which might otherwise develop.

Though hyperpyrexia is uncommon in measles, the fever sometimes requires attention. The effect of the fever upon the patient is a better guide for treatment than is the thermometer. If the child becomes rest-

less or delirious small doses of **acetphenetid** are admissible. Only enough should be given to reduce the temperature moderately and to allay restlessness. **Cold sponging** is the best treatment for high temperature and is far preferable to the administration of large doses of antipyretics.

According to Montefusco, good results are obtainable by the subcutaneous injection of **pilocarpine nitrate** in doses of 1 mgm. ($\frac{1}{16}$ grain), repeated as necessary. This method was found useful for the severe obstructive forms of laryngitis occurring during measles. Simonescu maintains that the active agent of measles and its toxin lose their pathogenic properties rapidly under the influence of **red light**, which exerts an abortive action on the disease and even benefits bronchopneumonia, when this complication is present.

The writer employed the following treatment with surprising results in the cure, and in the prevention of the spread of, both measles and scarlet fever, even in institutions, without adopting methods of isolation or disinfection. For twenty-seven years he has used pure **eucalyptus oil** in the following manner: During the first four days this oil is gently rubbed in, morning and evening, all over the body. The treatment is kept up until the tenth day of the disease. The tonsils and pharynx are swabbed with 1:10 **phenol** in oil every two hours for the first twenty-four hours, rarely longer. When this is begun early, secondary infections never occur and complications are unknown. If the treatment is carefully carried out, children may occupy the same room and even the same bed without risk of infection. No quarantine is necessary, and other children in the family may be allowed to attend school. No after-disinfection is required. Milne (Brit. Med. Jour., Sept. 2, 1911).

Case of extreme collapse in the course of measles which recovered after transfusion of 100 c.c. of **citrated blood** from a measles convalescent. The eruption was diffuse and ecchy-

mot, the fever up to 41° C., with collapse, anuria, incontinence and toxic dyspnea. After transfusion of 100 c.c. of blood from a man who had recovered from measles a week before, in two hours the vital functions had recuperated and speedy recovery followed. Ribadeau-Dumas and Brissaud (Bull. Soc. méd. des hôpitaux de Paris, Feb. 15, 1918).

A **specific curative action** in measles is exerted by **amidopyrin**. When this drug is given at the onset of the rash, there result a permanent reduction of temperature to normal or nearly normal within 12 hours; complete or partial inhibition of the rash; immediate euphoria, and disappearance of cough, coryza and conjunctivitis within a day or 2. No untoward effects were observed. The dosage is based on an adult dose of 12 grains (0.8 Gm.), the dose for children being derived from the formula: Age + 1, divided by 24. Three doses a day are given. M. Loewenthal (Brit. Med. Jour., July 12, 1924).

Uncomplicated cases do not require **stimulants**. Bronchopneumonia requires the same treatment that it would receive under other conditions. Other complications must be treated as they arise.

Phlyctenular conjunctivitis, with its array of dangerous complications, including ulceration of the cornea, is often witnessed in dispensaries as a sequel of measles. Textbooks do not lay sufficient stress upon the importance of keeping the lids **aseptic by careful cleansing**, and **not using the eyes** for reading, writing, etc., until the system has completely recovered from the debilitating influence of the disease.

Where pus in the eyes is noticed, a 10 or 15 per cent. **argyrol** solution should be instilled one or more times daily. To obviate gluing together of the lids, **petrolatum** may be applied to the lid margins in the evening.

During convalescence, unusual care should be exercised in **avoiding unnecessary exposure**. Tonics should be given freely. The various sequelæ should receive proper attention, and the particular susceptibility to tuberculosis should not be forgotten.

In an infant of 13 months the rash lasted only 1 day, and even **mustard packs** failed to bring it out again. The child's strength was kept up with **camphorated oil** and daily **glucose-adrenalin** injections. The condition growing constantly worse, a subcutaneous injection was made on the fifth day of 20 c.c. of **whole blood** from a brother who had had measles 6 months before. By evening the infant was playing in his bath, and he slept that night for the first time. The temperature began to go down, and by the next day the child was well. Terrien (Bull. Soc. méd. des hôp. de Paris, Dec. 26, 1919).

Large doses of **convalescent serum** were tried in 2 severe cases in which bronchopneumonia had developed; unmistakable improvement was manifest in 12 hours, 1 of these children being saved. Woody (Monthly Bulletin Department of Public Health, Philadelphia, Sept., 1924).

THEODORE LE BOUTILLIER,
Philadelphia.

MELANURIA.—The urine in cases of melanotic tumor at times contains melanogen, which upon standing or addition of oxidizing substances or alkalis changes into melanin, causing a blackish discoloration. Upon addition of ferric chloride, intensification of the shade may occur, or a black precipitate result which will dissolve in a solution of sodium carbonate. From this solution mineral acids will reprecipitate it. The black pigment may also occur in chronic malaria. S.

MENINGES AND BRAIN, DISEASES OF.—A number of the more important diseases of the brain and spinal cord are treated under special headings: **CEREBRAL ABSCESS;**

CEREBRAL HEMORRHAGE; MENINGITIS, CEREBROSPINAL; TABES DORSALIS, etc.

HYPEREMIA.

This alleged condition, also called "rush of blood to the head," is described in some textbooks, and is popularly spoken of as not uncommon. It is doubtful, however, whether it is to be recognized as a distinct clinical entity. Variations of the volume of blood in the brain doubtless occur, but the condition of hyperemia is probably but transient. It may presumably occur in persons who have impaired arteries. There is a sense of fulness in the head, flushed face, perhaps giddiness and mental confusion. A simple hyperemia, however, would not cause paralysis or loss of consciousness. On the whole, it is best not to elaborate the subject. Some of the symptoms ascribed to it are probably due to various toxemias.

ANEMIA.

Anemia of the brain occurs in various conditions; in fact, it may occur in so many conditions that it is to be regarded rather as a complication of other diseases than as a distinct disease in itself. Severe hemorrhage from any region of the body may cause it; also the withdrawal of large accumulations of fluid, such as ascites, which acts apparently by withdrawing blood from the vascular system generally. In many chronic wasting diseases there is deficient and impaired blood in the vessels generally, and some of the symptoms may be due to cerebral anemia. Such diseases are pernicious anemia, cancer, tuberculosis, and chronic Bright's disease; but in all such cases there is a cachexia, which probably accounts for the symptoms. Syncope, from what-

ever cause, is probably due to an interrupted blood-supply to the cardiac and respiratory centers. In arteriosclerosis there may occur transient symptoms, such as mental changes, even aphasia and paralysis, which are most readily explained by an interruption in blood-supply. No attempt will be made to describe cerebral anemia as a distinct affection, its symptoms being best considered in conjunction with the various diseases of which it is an occasional effect.

EDEMA.

Edema of the brain does not occur as a distinct disease. An edematous or "wet" brain is found in a number of grave organic affections, such as chronic alcoholism, paresis, etc., but it is then merely a terminal condition, and is best studied as a part of these affections.

ENCEPHALITIS.

DEFINITION.—By encephalitis we understand an inflammation of the encephalon, or brain. The encephalon properly includes the whole content of the cranium: thus the brain with its various subdivisions,—the hemispheres of the cerebrum, the mid-brain, the pons, the medulla, and the cerebellum,—together with the enveloping membranes, is included in the term. Brain abscess, although properly included in purulent meningoencephalitis, will not be discussed here, having already been considered under CEREBRAL ABSCESS (*q.v.*).

VARIETIES.—Among the forms of encephalitis other than purulent meningoencephalitis which will be briefly described are the so-called hemorrhagic encephalitis, and the circumscribed polioencephalitis of Wernicke and of Strümpell.

It must be understood that inflammation of the brain and its membranes is a process that occurs under many conditions and from numerous causes. The pus-forming micro-organisms are the common, if not the only, causes. Thus, in tuberculous meningitis there is usually some involvement of the cerebral tissue with formation of pus. In cerebrospinal meningitis, due to *Diplococcus intracellularis*, there is also a purulent exudate. Syphilis causes a specific meningocerebritis with a gummatous exudate.

One of the commonest causes of encephalitis is purulent otitis media, due usually to the streptococcus. Infection may arise also from purulent disease of other bones of the cranium, as of the nose and its accessory sinuses, and of the orbit. The resulting infection may lead to purulent meningitis, or to brain abscess, or to both. The pneumococcus, however introduced, may cause meningitis. Possibly other microbes will yet be observed to cause a similar infection. Trauma to the bones of the cranium may cause inflammation of the brain and its membranes, doubtless by secondary infection. A septic focus in any region of the body may cause secondary infection in the brain, but the commonest are abscess of the liver, ulcerative endocarditis, abscess of the lung, and empyema. In these cases the brain lesion is usually a metastatic abscess.

PURULENT MENINGOENCEPHALITIS.

Under this heading we shall describe the commonest form of inflammation of the encephalon, merely premising that in this affection the

membranes are usually involved along with the brain proper.

SYMPTOMS.—Chill, fever, headache, vomiting, convulsions, paralysis, rigidity, optic neuritis, and affections of consciousness are the chief symptoms.

Chill, or a succession of chills, sometimes occurs with an acute onset, but often the history of a rigor is not obtained. The onset may be rather gradual and insidious, without premonitions.

Fever is usually present, but its course is irregular. It may be accompanied with chills and sweating, and runs the usual course seen in sepsis.

Headache is commonly observed. It is either diffuse or marked by localized pain. In case of solitary abscess it is not always observed, but *per contra* it is sometimes intense. Its localizing value is not often great. Pressure may elicit tenderness, especially over and about the mastoid region in otitis media.

Vomiting is not uncommon. It often presents the type known as cerebral, in which the act of vomiting is propulsive, without nausea, and without reference to the presence of food in the stomach.

Convulsions are general or local, but they are not inevitable. The local convulsions are due to irritation of the motor centers, and are then localized in the limbs or muscle groups innervated from such centers.

Paralysis is usually a late manifestation, and is caused by involvement of the motor cortex or by pressure on the subcortical tracts, or the descending motor fibers. It may be *focal*, *i.e.*, located on one side, or in one limb, or even in a few muscle groups, according to the area of the brain involved.

Focal convulsions are very likely to be followed by focal paralysis. Paralysis of the eye muscles is sometimes caused by involvement of the third, fourth, and sixth nerves in the inflammatory process.

Rigidity, as a sign of meningeal irritation, is sometimes observed, especially about the nuchal region. It is occasionally seen in one or more limbs.

Optic neuritis, or choked disk, is an important symptom. It may progress rapidly and threaten the integrity of the nerve. It is not always present, but, when present, is a most significant symptom. If the pus formation is rapid, especially at the base, optic neuritis is very likely to occur.

Consciousness is affected in various ways and degrees, from a slight stupor or delirium to maniacal excitement, passing into coma.

The course of the disease varies. It is sometimes rapid or fulminating. On the other hand, cases occur of infection of the membranes, as in otitis media, in which the duration is prolonged and marked by exacerbations and remissions.

PATHOLOGY.—In purulent meningitis the membranes, especially the pia-arachnoid, are thickened and opaque, and pus is diffused beneath them. This pus is observed especially at the base, but it sometimes also spreads along the lateral aspects, and may even be seen on the convexity. It often follows along the course of the blood-vessels, extending into the fissures, and appearing as white streaks. The underlying cerebral substance is usually somewhat involved, and may be softened, edematous, and broken down in places. Thrombi may form in the sinuses, and occasionally

engorgement of the veins on the outside of the skull is observed. The writer saw this condition recently in a case of infection from the sinuses of the nose. The collection of pus may be so great, especially at the base, as to present the appearance of a diffuse abscess, and in some cases an abscess cavity may form in the brain-tissue. When purulent meningitis arises from otitis media or from disease of the nasal cavities or orbit, the direct connection is usually easily traced, the inflammation having spread as from a center.

DIAGNOSIS.—It is not always possible to distinguish purulent meningocerebritis from brain abscess; in fact, as can readily be understood, the two conditions merge into each other. Solitary abscess, in which the pus is well walled off, is usually a more insidious and a more protracted disease, and the focal symptoms, such as paralysis and convulsions, are more marked. In diffuse purulent meningoencephalitis the onset is often acute and the progress rapid, focal symptoms are less marked, and the general symptoms, such as pain, fever, and delirium, are more pronounced.

Tumor of the brain is likely to simulate abscess rather than diffuse meningoencephalitis. The clinical history in tumor is different. The onset is insidious, the course slow, and the localizing symptoms more conspicuous. There is no history nor evidence of infection.

Cerebral hemorrhage occurs abruptly; pain and fever are not early or marked symptoms, and hemiplegia is usually seen from the beginning, except, of course, in the somewhat rare cases in which the motor regions are not involved.

Cerebral symptoms due to uremia may be simulated by this disease, but the history of the case, the condition of the urine, and the presence or absence of a focus of infection are the data necessary for differentiation.

Lumbar puncture may reveal the presence of pus or blood-cells in the cerebrospinal fluid in all cases of infection of the encephalon.

What we call meningeal symptoms in reality are not meningeal. In an acute case, a young woman had had fever and diarrhea for two weeks; coma developed, with slight trismus and slight contracture of the arms and exaggeration of the tendon reflexes. The legs were relaxed, the tendon reflexes abolished. There was no Kernig's sign nor trace of hyperesthesia or convulsions. Lumbar puncture released limpid fluid under considerable pressure. There was nothing to suggest poisoning, and the temperature kept very high. The woman died the third day after the onset of the coma, and necropsy revealed merely acute encephalitis without suppuration, as the only lesion accompanying the septicemia. Creyx (*Jour. de Méd. de Bordeaux*, Mar., 1918).

PROGNOSIS.—This is very grave unless the patient can be promptly relieved by surgical intervention.

TREATMENT.—There is no successful treatment for this condition with drugs. We know of no medicine that can control in the slightest degree the course of purulent meningoencephalitis. We are driven to palliative measures only, and even these do not accomplish much. Mercury and the so-called alteratives are useless. Opium, especially in large doses, only covers up the trouble for a time, and in advanced cases, with delirium and a tendency to coma, it is even dangerous. All other sedatives, such

as chloral, the bromides, and the coal-tar products, are of doubtful benefit. An ice-bag to the head may relieve pain, and it does no harm.

The one remedy is to get at and **evacuate the pus** as early as possible. In otitis media this is not infrequently done with success.

Four cases of acute toxic meningo-encephalitis of otorhinologic origin. This condition has not infrequently been mistaken for otitic brain abscess—a diagnostic error resulting in unnecessary intracranial exploration. In acute toxic meningoencephalitis timely **drainage of the focus of infection** yields a cure. Preoperative diagnosis of this condition indicates at once the form of surgical procedure required. Yerger (*Arch. of Otolaryng.*, Feb., 1925).

ACUTE HEMORRHAGIC ENCEPHALITIS.

Some observers have described a form of encephalitis to which they have given the above name. According to Oppenheim the cause is always, or in most cases, some form of infection. Thus, influenza, measles, scarlet fever, typhoid fever, pneumonia, erysipelas, whooping-cough, mumps, and diphtheria have all been accused of causing this affection.

The disease is characterized by multiple foci of congestion and by minute and even massive hemorrhages in the tissue of the brain. Infiltration of leucocytes, small emboli, and areas of necrosis are seen. The membranes, as a rule, are not involved. These lesions seem to point to the local action of micro-organisms or their toxins.

SYMPTOMS.—These are usually well marked, and consist of headache, vomiting, convulsions, delirium, and various paralyses. The constitutional reaction is featured by prostration

and rapid pulse, but fever is said to be not always conspicuous. Coma supervenes, with rapid respiration and a tendency to death. Recovery has been claimed in some cases.

PROGNOSIS.—This is grave.

DIAGNOSIS.—The disease simulates meningitis, and, indeed, cannot always be distinguished from it. Moreover, the distinction is not of practical clinical importance. This complication of encephalitis may be suspected in cases of any of the infectious diseases named when grave cerebral symptoms set in.

TREATMENT.—This is symptomatic. The attempt should be made to relieve pain, as well as to combat the rapid lethal trend.

Bromides or other sedatives may be given for restlessness, an ice-bag applied to the head, and calomel and methenamine administered.

Of 2 cases of acute hemorrhagic encephalitis of the cortex, 1 recovered following treatment with **mercurochrome-220** soluble. Wilkerson (*Texas State Jour. of Med.*, Oct., 1925).

In 3 cases of encephalitis following typhoid fever prompt recovery took place after intravenous injection of **gentian violet**. The efficacy of this measure in each instance seemed evident, as no other change in the treatment was made. Visher (*Jour. of Nerv. and Ment. Dis.*, Oct., 1925).

ACUTE ANTERIOR POLIO-ENCEPHALITIS.

Strümpell described an acute inflammatory process, localized in the motor areas of the cerebrum, which has been called acute anterior poli-encephalitis. The anatomical picture is not unlike that described in the preceding section. Infantile cerebral palsy may result from the affection. Some writers claim that this cerebral infection occurs occasionally in the

epidemic form of acute anterior poliomyelitis, but in the epidemic in New York not much appears to have been observed to confirm this view.

According to some German observers, acute anterior polioencephalitis leads to cerebral sclerosis, a terminal condition which is sometimes found in the brains of children who have suffered with cerebral palsy.

SYMPTOMS.—These vary according to the location and extent of the lesion.

Hemiplegia, monoplegia, diplegia, and even paraplegia are the various types of paralysis observed, and in young children epilepsy, speech defects, and arrest of mental development are among the results. The paralysis is of spastic type, with exaggerated reflexes, and without true muscular atrophy.

ACUTE SUPERIOR AND INFERIOR ENCEPHALITIS.

Wernicke called attention to a very grave acute destructive process, which is localized about the aqueduct of Sylvius and the ependymal gray matter of the third ventricle. This form of acute encephalitis is claimed to occur especially in alcoholic subjects, but it also probably occurs from some forms of infection. In the region just named the disease is called *superior* polioencephalitis; but a similar acute affection occurs about the floor of the fourth ventricle, involving the pons and medulla, and is then called *inferior* polioencephalitis, and is practically an acute bulbar palsy.

In these various regions the gray matter, especially the nuclei of the cranial nerves, is involved, and the affection has thus some affinity with the process in the spinal cord called

acute anterior poliomyelitis. In the midbrain and pons, however, other areas are also sometimes involved, so that the clinical picture may include more than a mere nuclear palsy.

SYMPTOMS.—In the *superior* form the onset is often sudden and the course rapidly fatal. Delirium or stupor may occur, and the various muscles of the eyes are paralyzed, presenting various forms of ophthalmoplegia. Among other symptoms are nystagmus, optic neuritis, and even tremor, ataxia, and paralysis of the limbs. Articulation may be affected, and facial palsy has been seen. The pulse fails rapidly, and the tendency to death is marked. The prognosis is very grave, and the treatment must be sustaining.

In the *inferior* form of this disease we see an acute bulbar palsy, with paralysis of the lips, tongue, and muscles of mastication and deglutition. The extremities may be involved, the deep reflexes exaggerated, and respiration and the pulse accelerated.

These various forms differ according to the extent of the lesion. Symptoms are accordingly grouped in various ways. Prostration is likely to be extreme, and there is usually some febrile reaction. The paralyzed muscles are flaccid when the nuclei are entirely involved, and the electrical reactions are changed.

DIAGNOSIS.—The diagnosis rests largely upon the nuclear paralysis of the various cranial motor nerves; but, as already said, the process in some cases may be more widely diffused through the midbrain, pons, and medulla, in which case motor and sensory tracts may be affected as well as the nuclei of these nerves.

EPIDEMIC (LETHARGIC) EN-CEPHALITIS.

DEFINITION.—An infectious disease of unknown causation, involving various portions of the nervous system, but especially the basal ganglia, pons and medulla, and usually attended with somnolence or stupor.

SYMPTOMS.—As described by Netter the victim is seized with fever, headache, and at times vomiting. Marked lassitude and somnolence soon develop. At first the patient can be momentarily roused from his slumbers, but later the condition passes into an actual coma, occasionally interrupted by delirium and restlessness. Very characteristic are the ocular disturbances, usually bilateral, consisting of ptosis, strabismus, immobility of the eyeball, or nystagmus. The intrinsic ocular muscles are less frequently involved, but paralysis of accommodation and a sluggish light reflex have been observed. The muscles innervated by the facial and those of the tongue, larynx, and extremities may participate in the paralysis. Tremor is not exceptional. Death or recovery may occur within a few days, but generally the disease persists through weeks or months. Lassitude and the eye disturbances continue for some time during convalescence.

While the combination of somnolence, asthenia and cranial nerve involvement is characteristic when present, accumulated experience has shown that the symptoms vary widely, even in the same patient at different times. Not a few patients exhibit restlessness and insomnia rather than lethargy; or, these manifestations may appear in succession. Periods of diplopia or

blurred vision at times constitute the earliest symptom, and vision may even be temporarily lost. In some cases motor symptoms are conspicuous; these may comprise various myoclonic contractions, tremors of various types, muscular hypertonicity, slow movements, a mask-like face, various paralyses or pareses, and slow, hesitating or indistinct speech. Changes in the reflexes are variable. The Argyll-Robertson pupil may be present.

The onset is more often gradual than sudden.

A myoclonic form of the disease described. After about a week of malaise and slight fever, there appear brief, explosive muscular contractions of the limbs, face, and diaphragm (epidemic hiccough), sometimes localized in 1 portion of the body. Insomnia is present, and lethargy and eye symptoms absent. About the third week delirium appears. In the terminal stage, lasting 3 or 4 days, speech becomes difficult and jerky, and there are automatic gestures, lessened intensity of the myoclonic seizures, followed by coma and death. Sicard and Kudelski (*Bull. Soc. méd. des hôp. de Paris*, Jan. 29, 1920).

The writer himself experienced, in particular, a peculiar hyperesthesia of the scalp and upper part of the face. W. Boyd (*Quart. Jour. of Med.*, Jan., 1925).

Among other symptoms the author witnessed a scarlatinoid rash, desquamation from the hands and forearms, a myxedematoid condition of the hands, xanthochromia, hemiatrophy of the tongue, and attacks of hemispasm and hemiataxia. E. Trömmner (*Deut. med. Woch.*, Jan. 16, 1925).

ETIOLOGY.—A relationship of this disease to influenza has been commented upon, a considerable number of cases, but by no means all, having a history of this infection. Kaiser-Petersen found that in 8 influenza

epidemics between the years 1580 and 1833 there had always been cases with symptoms of lethargic encephalitis.

According to Levaditi, the saliva virus, that of herpes and that of encephalitis are variants of a single filtrable virus. Encephalitis develops when its virulence for some reason becomes enhanced and it passes through an inflamed nasopharyngeal mucosa to invade the central nervous system.

The writer reports having isolated somewhat peculiar streptococci constantly from infected tonsils, teeth or nasopharynx during life in 81 cases, and from the brain after death. After as many as 44 subcultures and a series of animal passages, characteristic symptoms and lesions of different forms of encephalitis were reproduced in animals. E. C. Rosenow (Jour. of Inf. Dis., Apr., 1924).

Investigations of Loewe and Strauss, supported by Thalheimer, led to the conclusion that the virus is a minute filtrable body which, injected in rabbits, induces a disease clinically similar to the human disorder. The organism was cultivated on ascitic fluid tissue medium from brain material and spinal fluid from human patients.

There has been an impression that the disease is mildly contagious. J. Lépine ascribes the low degree of transmissibility to a lack of receptivity on the part of the nervous system of contacts, and calls attention to the almost invariable predisposing factors in his 50 cases, *viz.*, excessive physical or emotional strain, a general nervous or mental taint, a tendency to migraine, or the menopause. Healthy carriers of the disease are believed to occur.

In 451 cases analyzed by Neal, Jackson and Appelbaum the greatest number

of cases—in the years 1918 to 1923—occurred in the first 3 months of the year (203 cases) and the smallest number in the summer months (68 cases). In this series no less than 217 cases were less than 15 years of age. There were 7 over 60 years old. There is a moderate excess of male over female patients (about 3 to 2).

PATHOLOGY.—The main changes found in fatal cases are, according to Bramwell: Edema of nerve tissue; infiltration of nerve tissue and perivascular lymph sheath with cells, usually lymphocytic in type, and proliferation of neuroglia. These changes he found most striking in the ventral portion of the pons, especially in the region of the substantia nigra, implicating the fibers of the third nerve. Walshe associates many of the symptoms with a selective action on the basal ganglia and certain motor nerves in the brain-stem, producing the familiar basal ganglia and mid-brain types of the disease. In its irritative effect the virus seems to act equally on any and every part of the nervous system, from cerebral hemispheres to spinal roots; hence the varied clinical symptoms and difficulty of classification. Changes in the pituitary body have been noted by some and been considered to account for the characteristic hypersomnia.

The changes most constantly visible to the naked eye consist of pial injection and, at times, areas of meningitis and small hemorrhages.

DIAGNOSIS.—The most prominent symptoms, according to Neal, are fever, vomiting, headache, malaise and drowsiness or delirium. Aside from the eye symptoms, when present, katatonia may be observed. Kernig's

sign is not common unless associated with spasticity.

The disease has been misdiagnosed, among other conditions, as poliomyelitis, cerebral hemorrhage or thrombosis, brain abscess, meningitis, neurasthenia, botulism, and acute paralysis agitans.

In the distinction between encephalitis and poliomyelitis, Bassoe stresses the greater tendency to Kernig's sign and stiff neck and back in the latter disease. Some authorities believe that cases diagnosed in the past as the encephalitic type of poliomyelitis were in reality cases of epidemic encephalitis.

From tuberculous meningitis the diagnosis is best made by the spinal fluid, as the clinical features may be misleading. From cerebral hemorrhage, and especially thrombosis, differentiation may be very difficult; a hemorrhagic fluid points rather to cerebral hemorrhage. Distinction from brain abscess or tumor is often achieved only after extensive X-ray studies or at autopsy. Central nervous syphilis calls for a Wassermann test. In dementia precox simulating encephalitis, observation for a considerable time may be necessary for differentiation (Neal).

Only in a few instances did the writers find a normal cerebrospinal fluid. The fluid is usually clear and increased in amount; sometimes it is slightly hazy, and at times yellowish or even blood-tinged. The cells are usually slightly or moderately increased, the cell count being ordinarily below 100, with a preponderance of mononuclears, though occasionally up to 1000 or more. Nearly always there was a slight or moderate increase in albumin and globulin. Fehling's solution is promptly and well reduced. Bacteriologically the fluid is sterile.

These findings are characteristic but not pathognomonic. Increase in sugar content does not certainly indicate encephalitis, being also found occasionally in poliomyelitis, central nervous syphilis, and even meningism. It is most helpful in differentiating tuberculous meningitis, in which, when well advanced, the sugar is usually greatly diminished. Where there is suspicion of syphilis, the Wassermann is the most significant test. The blood is not characteristic in encephalitis; there is usually a leukocytosis of 10,000 to 15,000; blood cultures are sterile. J. B. Neal, H. W. Jackson and E. Appelbaum (*Amer. Jour. Med. Sci.*, Nov., 1925).

SEQUELÆ.—Grossman, in 89 cases, noted some disturbance of psychic functions in 55 per cent.; insomnia, 55 per cent.; tremor and involuntary movements, 58 per cent.; residual signs in cranial nerves, 64 per cent.; altered deep reflexes, 30 per cent., and pupillary disturbances, 30 per cent.

Other sequelæ reported include deficient convergence, optic atrophy (rare), headaches, neuritic pains, marked salivation, weakness and paralyses, gastrointestinal and bladder disturbances, nocturnal mental disturbance or delirium, spasmodic forced and rapid breathing, spastic conditions, vomiting, headaches, transient obesity, diabetes insipidus, pituitary adiposis with polyuria and genital atrophy, seborrhea of the face, and altered disposition—the latter marked by quarrelsomeness, incorrigibility, indolence, sometimes mannerisms and stereotyped movements, a silly cheerfulness, etc.

Much stress has been laid on the parkinsonian syndrome which sometimes follows the disease. The tremor may be confined to one arm or foot.

It may appear even 2 years after the encephalitic disorder.

Attention directed to cases with somnolence and fatigability by day but insomnia with much greater capacity for work, better concentration and handwriting, etc., by night. Sabatini (Policlin., Jan. 1, 1923).

PROGNOSIS.—The duration of the symptoms is very variable; some patients seem completely recovered in a week or 2, while in others the condition persists many months. At times it follows a chronic course, with alternate remissions and exacerbations; or, it may suggest an acute disorder at first, then pass into chronicity. Relapses with acute manifestations may occur after long periods of apparent health.

In a series recorded by Neal the mortality in adults was 27.54 per cent. and in children 28.14 per cent.

TREATMENT.—No dependable treatment has been discovered, although a variety of procedures have been asserted beneficial by individual observers. **Lumbar puncture** and withdrawal of spinal fluid to relieve pressure, up to 40 or 50 c.c., is the most widely accredited measure, and in some instances has been strikingly beneficial. According to Hauser there is sometimes permanent improvement after but 1 puncture. Usually repeated punctures are carried out, at intervals varying with the effects observed and the clinical condition, including pressure symptoms. In cases with excitement, **phenobarbital** is a serviceable palliative.

According to Cheinisse (Presse méd., Feb. 19, 1921), Netter advocates the **fixation abscess**, induced by 1 or 2 c.c. of old turpentine in the subcutaneous tissue of the abdominal wall. He also gives **methenamine**

by mouth in declining doses of from 2 to 1 Gm. (30 to 15 grains) daily, and for asthenia, 3 or 4 drops of **adrenalin** solution every 3 hours. Rucks (Jour. Okla. State Med. Assoc., Oct., 1922) observed cessation of convulsions in an acute, maniacal case after intravenous injection of 100 c.c. of 15 per cent. **hypertonic salt solution**.

C. K. Russel (Canad. Med. Assoc. Jour., Oct., 1922) reported good results from subcutaneous injections of **horse serum**, including **diphtheria antitoxin**. The dosage was 10 to 20 c.c. H. F. Helmholtz and E. C. Rosenow (Jour. Amer. Med. Assoc., Dec. 16, 1922) report 3 cases of manifest benefit from **lumbar drainage** and a **specific serum** prepared by Rosenow, given intravenously in doses of 5 to 20 c.c.. Courcoux and Meignant (Bull. Soc. méd. des hôp. de Paris, May 8, 1924) noted rapid improvement in a patient given 6 daily intravenous injections of 4 Gm. (1 dram) of **sodium salicylate** in a 4 per cent. solution, and subsequently, the same amount intramuscularly.

Agostini (Policlin., July 21, 1924) injects 0.15 to 0.5 Gm. of **neoarsphenamin** at weekly intervals. Visser (Northw. Med., June, 1924) advocates intravenous injection of 10 c.c. of 1 per cent. **mercurochrome** in freshly distilled water. E. Matthew (Lancet, June 7, 1924) injects 4 c.c. of 25 per cent. **magnesium sulphate** intramuscularly at intervals of 12 and later 24 hours, arresting the myoclonic and choreo-athetotic movements.

C. E. Riggs (Minn. Med., Oct., 1923) favors **lumbar puncture** and **sodium iodide** intravenously. J. H. Leiner (N. Y. State Jour. of Med., Dec., 1923) urges persistent non-specific therapy by **sodium nucleinate**.

Neustaedter, Hala and Banzhaf (N. Y. State Jour. of Med., Jan., 1924) gave intravenous injections of 20 to 30 c.c. of **immune antipoliomyelitis horse serum**, with recovery of 23 out of 30 serious cases. F. Stern (Med. Klin., July 27, 1924) injected 50 to 80 c.c. or more of **convalescents' serum** intramuscularly; of 27 acute or subacute cases, but 1 died. R. W. Power (Brit. Med. Jour., June 28, 1924) witnessed relief from pain and spasms following 2 injections of 10 c.c. of the patient's **spinal fluid intravenously**, 24 hours apart.

Regarding the treatment of sequelæ, following are some of the

measures suggested: **Sedatives** when required; **tonics** and **change of environment**; **iodides** for motor or psychic sequelæ; **active** and **passive movements** for spastic paralysis; **tepid baths**, **spinal counterirritation** and **diet** for sudden flare-ups, and **scopolamine hydrobromide**, $\frac{1}{150}$ grain (0.0004 Gm.), with **codeine sulphate**, $\frac{1}{4}$ grain (0.015 Gm.), 3 times a day for parkinsonian tremor.

Definite, though not permanent, improvement of the parkinsonian condition noted under ascending doses of **atropine sulphate**, beginning with 0.0005 Gm. ($\frac{1}{30}$ grain) 4 to 6 times a day in pills for 3 to 6 days, then gradually increased to as high as 0.004 Gm. ($\frac{1}{8}$ grain), with intervals of 2 or 3 days between courses. Szyszka (Münch. med. Woch., Jan. 12, 1923).

Patients with parkinsonian symptoms receive most benefit from **scopolamine**. If given subcutaneously, a start can be made with $\frac{1}{150}$ grain (0.0004 Gm.) once a day, to be later increased, if necessary, up to $\frac{1}{60}$ grain (0.0013 Gm.). If given by mouth, larger doses may be given thrice daily, just after meals. The former method seems to act the more powerfully and persistently. McCowan, Harris and Mann (Brit. Med. Jour., May 1, 1926).

MENINGITIS (PACHYMENINGITIS; LEPTOMENINGITIS).

DEFINITION.—Inflammation of the membranes of the brain. This may arise from various causes and is a symptom of various diseases. Thus there are purulent meningitis, tuberculous meningitis, syphilitic meningitis, and meningitis due to the pneumococcus. It is usual to distinguish between inflammation of the dura mater, which is called *pachymeningitis*, and inflammation of the pia mater, which is called *leptomeningitis*. But practically the two membranes are often involved together.

Inflammation of the dura may occur as a septic infection, as in fracture or injury to the bones of the skull or in otitis media. It is then purulent. This condition is not easily distinguished from cerebral abscess and from purulent meningoencephalitis (*q.v.*). A distinct form is the *pachymeningitis hæmorrhagica* of Virchow, in which there is a hematoma of the dura, with the appearance of an organized blood-clot. It occurs especially in chronic alcoholics and the chronic insane. It is of vascular rather than inflammatory origin.

Inflammation of the pia mater, or *leptomeningitis*, likewise occurs from various causes. Thus there are tuberculous meningitis, epidemic cerebrospinal meningitis (see **MENINGITIS, CEREBROSPINAL**), and syphilitic meningitis. Various other forms are observed, but they are best studied in conjunction with the diseases in which they arise. Thus there is purulent meningitis (see **PURULENT MENINGOENCEPHALITIS**, in this article) and there are meningitides due to the pneumococcus and other germs, including the influenza and the colon bacilli.

SYMPTOMS.—The symptoms are headache, vomiting, optic neuritis, fever, stiffness of the neck and back, rigidity of the limbs, and increased reflexes, followed in time by delirium, coma, convulsions, and death.

The vomiting in meningitis is peculiar in being generally unassociated with nausea and retching. In basal meningitis it is particularly frequent. The headache is persistent and severe, and, though usually frontal, it may be referred over the entire head. Convulsions occur oftenest in tuberculous meningitis in children. Retraction of the head and neck rigidity are most

pronounced where the basal meninges and, particularly, those of the spinal cord are involved. Optic neuritis is usually a late symptom. Other more or less common symptoms are ptosis, strabismus, contraction and later dilatation of the pupils, temporary pupillary inequality, and some of the characteristic phenomena of involvement of the trigeminal, facial, special sense, and cutaneous nerves.

DIAGNOSIS.—Aside from the symptoms already referred to, knowledge of the existence of some antecedent condition commonly a cause of meningitis, *e.g.*, tuberculous disease, otitis, or pneumococcus infection, will not infrequently be of diagnostic assistance. Persistent headache, convulsions appearing only at a relatively late stage, and ocular involvement are suggestive rather of true meningitis than of meningeal manifestations in the course of a general infectious process. Lumbar puncture is frequently of great value; through it the existence of a leukocytic reaction can be shown and the particular micro-organism responsible ascertained by smears and cultures.

Brudzinski's sign in meningitis consists of reflex actions manifested in what are called the neck sign and the leg sign, and comprises two reflex phenomena, the identical reflex (*réflexe identique*) and the contralateral reflex (*réflexe contralatérale*).

The former is elicited by forcibly flexing the head on the chest, when the arms and legs are drawn up, to remain thus.

The contralateral reflex is produced by passive flexion of one leg, which causes the limb of the opposite side to draw up and remain in the same position.

Among 42 cases of meningitis Northrup found the neck sign positive in 97 per cent.; the leg sign in 66 per cent.; Kernig's sign in 57 per cent., and the Babinski sign in 50 per cent.

Minervini finds the *ankle sign* of meningitis of diagnostic value. The ankle is grasped with one hand, the toes with the other, and the foot bent up toward the knee with a forcible push. When the phenomenon is not present the foot drops back again as soon as it is released, but in case of the pathognomonic reflex contraction, the flexion persists. This ankle tonus is often in inverse proportion to the knee-jerk. It may be encountered in meningitis, sciatica, spastic tabes, and hysteria.

Meningism comprises the syndrome: Fever, rigid neck, hyperesthesia, headache, Kernig's sign, etc.; but the lumbar puncture is sterile. Nearly all acute infectious diseases show some percentage of meningism. That for scarlatina is 4 per cent. It sometimes occurs in helminthiasis, and a hysterical type is known. It is usually completely recovered from. The lesions comprise hyperemia and edema. The treatment is symptomatic. Kayser (Berl. klin. Woch., June 3 and 10, 1913).

Mild pressure on the dorsal wall of the external auditory meatus in meningitis causes severe pain and a marked reaction, even during stupor. The negative control is made by pressure on the anterior wall. The author calls this sign the "*auricularis phenomenon*" and considers it an early symptom of otitic meningitis. B. Mendel (Klin. Woch., Apr. 23, 1923).

In 5 cases of *influenzal meningitis* no typical clinical picture could be discovered, and examination of the spinal fluid alone gave the diagnosis through the Gram-stained slide, the indol test, and the cultural characteristics of the bacilli. Greenthal and G. F. Kelly (Wis. Med. Jour., Sept., 1924).

In the differential diagnosis, brain tumor may at times give trouble, the more rapidly growing tumors being confused with acute leptomeningitis, and the more slowly, with the chronic form. Optic neuritis, however, is apt to be more pronounced and progress further in brain tumor, while symptoms such as pupillary inequality

and strabismus suggest tumor. In hysteria there is absence of fever.

PROGNOSIS.—Recovery is uncommon except in syphilitic meningitis, in which antiluetic specifics are applicable, and in epidemic cerebrospinal meningitis, in which serum treatment lowers the mortality. Of 30 patients with pneumococcal meningitis seen by Rolly, 4 recovered.

TREATMENT.—Surgical treatment is indicated in suppurative meningitis of otitic origin. Stacke regards lumbar puncture as the key to successful treatment in cases of meningitis propagated from the middle ear by way of the labyrinth, and advises its performance whenever vomiting comes on in suppurative ear disease, especially if accompanied with vertigo, fever, or intense headache. Indeed, the radical operation is indicated, he states, in the presence of these symptoms even if the cerebrospinal fluid is found clear, and if the severe morbid manifestations do not promptly subside the labyrinth should be operated at once.

In otitic meningitis the writer practices craniotomy, particularly in the middle cranial fossa. If the dura shows no signs of a deep morbid process, he goes no further. Repeated lumbar puncture not only allows oversight of the course of the meningitis, but relieves the pressure, and is directly curative. He has also found an *anti-streptococcus serum* useful. Recovery is the rule in otogenous meningitis when the primary focus is not too close and pleocytosis is slight or moderate. After removal of the primary focus, the meningitis subsides. But there is no arresting a fulminant meningitis. Holger Mygind (Ugeskr. f. Læg., Aug. 2, 1923).

Where operative indications do not exist, the treatment of meningitis, except in the syphilitic and epidemic

forms, can be little more than symptomatic. Elevation of the head and the application of ice to it are considered useful. The use of blisters, applied to the back of the neck, is likely to prove of value. The patient must be kept in an absolutely quiet and preferably darkened room. A light, fluid diet should be given.

Headache may be combated with analgesics, and fever with cool sponging or bathing. Internal use of methenamine in full doses has been recommended. Arnold found that for continuous vomiting in protracted cases hydrochloric acid is very beneficial, morphine, on the contrary, aggravating this symptom. Inunctions of mercury have long been considered useful in non-tuberculous meningitis cases. Relief of excessive intracranial tension by lumbar puncture has seemed valuable. In staphylococcal meningitis Churchill has used an autogenous vaccine apparently with complete success.

Case of skull fracture followed by meningitis in a child aged 5 years. Spinal fluid cultures yielded *Streptococcus mucosus*. Treatment by ethylhydrocupreine (optochin) hydrochloride and antipneumococcus serum was successful, the former injected intraspinally, 0.03 Gm. ($\frac{1}{2}$ grain) in 10 c.c. ($2\frac{1}{2}$ drams) of distilled water, and the latter intravenously in a 40 c.c. dose. Cordua (Berl. klin. Woch., Nov. 7, 1921).

Case of diffuse purulent leptomeningitis (*S. hemolyticus*) secondary to abscess of otitic origin. The prognosis in otitic meningitis is very unfavorable (6 recoveries out of 71 cases—Breiger). Many authorities favor a mastoid operation or labyrinthectomy. In the author's case lumbar puncture under general anesthesia with removal of the needle only when 1 drop appeared in 3 seconds, was alone carried out, and complete recovery occurred in 8 weeks. Shaw (Arch. of Ped., Jan., 1924).

Early continuous drainage of the *cisterna magna* advocated for meningitis of staphylococcic or streptococcic origin. Continuous drainage by this route is easier to maintain than by the lumbar route. It is relatively simple to immobilize a drainage tube in the hollow of the neck by a large dressing. The tube is connected with a bottle and the latter, if the patient is very restless, inserted into the dressing. Three of 4 cases thus treated survived, comprising 1 each of infection by *Streptococcus viridans*, *S. hemolyticus* and *Staphylococcus aureus*. Dandy (Surg., Gyn. and Obst., Dec., 1924).

Favorable results in otogenous meningitis from intraspinal injections of *pneumococcus serum* in addition to surgical treatment. Missorici (Pediatrics, Feb. 15, 1925).

Serous meningitis, described by Quincke, is characterized by involvement of the pia-arachnoid. The symptoms are mild, and are chiefly fever, headache, stiffness of the neck, increased reflexes, and occasionally optic neuritis. The cause is doubtful, but syphilis may be suspected and should be tested for.

SPINAL MENINGITIS.

Inflammation of the membranes of the spinal cord may be located either in the dura or in the pia, or, as is not uncommon, in both. Syphilis is a common cause of meningomyelitis, in which either one or both membranes may be involved. Tuberculous meningitis is much more rare than the same condition in the brain, but the membranes may be involved in tuberculous spinal caries. Cerebrospinal fever is an acute infection, described elsewhere (*q.v.*). A purulent meningitis occasionally occurs from a septic focus, distant or remote, and spinal meningitis may be caused by the pneumococcus.

HYPERTROPHIC PACHYMEINGITIS.

This occurs especially in the cervical region, and is usually caused by trauma. The dura is much thickened and the cord is involved. The symptoms, as pointed out by Lloyd, closely resemble those of syringomyelia.

It is practically not possible in many cases to distinguish a pure meningitis from a meningomyelitis, or a leptomeningitis from a pachymeningitis. The various conditions should be studied in the various diseases which cause them, as in tuberculous meningitis, cerebrospinal meningitis, and syphilis (*q.v.*).

TUBERCULOUS MENINGITIS.

This condition is most marked at the base of the brain, where the membranes become thickened and opaque and an inflammatory exudate occurs. It is most common in children.

SYMPTOMS.—These may be divided into three stages:—

In the first stage there are headache, vomiting, constipation, slight fever, and a general decline in health, with slight mental changes, as irritability. The onset is insidious, but in some cases it may be abrupt. The headache may be accompanied by the so-called *hydrocephalic cry*, occurring especially during sleep.

In the second stage the disease is well marked. There are delirium, retraction of the head, fluctuating temperature, slow and irregular pulse, obstinate constipation, convulsions, optic neuritis, and various paralyses, *e.g.*, ocular, or even a hemiplegia.

In the third stage there are coma, weak and rapid pulse, sometimes a hypothermia, incontinence, and convulsions, and paralysis may persist.

DIAGNOSIS.—In the early stage the disease may be mistaken for infantile convulsions, gastrointestinal disorders, or a simple febrile attack. Later it may simulate pneumonia, typhoid fever, poliomyelitis, epidemic encephalitis, or influenza. It may simulate a few other disorders, but the resemblance is slight. The distinction is to be made by the gradual predominance of the brain symptoms, and by eliminating the distinctive symptoms of such diseases as pneumonia and typhoid fever. Lumbar puncture should be availed of; the fluid is generally only slightly turbid, but often contains small floculi of fibrin; the cells are nearly all mononuclear, and tubercle bacilli can sometimes be demonstrated. The Pandy test has been recommended (see under CEREBROSPINAL FLUID, Vol. III), a negative result as a rule excluding tuberculous meningitis. In the second stage it is scarcely possible to mistake the disease.

In 66 cases in children, fever was an early symptom in 51; cough in 23; headache in 11; vomiting in 10; constipation in 9; stupor and anorexia in 8 each. The Pirquet reaction gave 100 per cent. positive at the beginning; in the second stage, 61 per cent., and in the last stage, 20 per cent. The globulin test of the spinal fluid was positive in all. In most cases the albumin was increased, the highest being 0.23 per cent. and the lowest, 0.0165 per cent. The small lymphocytes were generally greatly increased. The polymorphonuclears came next, and the relation with the large lymphocytes was as 2:1:0.2. Tubercle bacilli were present in 70 per cent., though usually absent at the beginning. Kaneko (Jour. of Orient. Med., Nov., 1923).

TREATMENT.—The treatment is unsatisfactory. The measures already mentioned for the treatment of other

forms of meningitis are also applicable in the tuberculous variety.

Successful treatment of 2 cases of basal meningitis by **iodoform inunction**. An ointment was made up containing 15 grains (1 Gm.) of iodoform to the ounce (30 Gm.) of petrolatum, and rubbed thoroughly into the back and posterior part of the scalp, night and morning. Small doses of **potassium iodide** and **bromide** were also given. Mowat (Lancet, Jan. 7, 1911).

Repeated intraspinal injections of oxygen gas (artificial pneumorachis) seemed to produce favorable results in a few cases. The writer first allowed as much spinal fluid to escape as would flow through the needle, then injected slowly 5 to 10 c.c. of oxygen with a 20 c.c. Luer syringe, allowed froth to escape, and repeated the injection. E. A. Sharp (Arch. of Neurol. and Psych., Dec., 1921).

Forty-five cases of recovery are on record, all authenticated by the finding of tubercle bacilli in the spinal fluid or by guinea-pig inoculation. Only 1 child below 2 years recovered. Various observers claimed good results for **repeated lumbar puncture**, **decompression**, **Bier's hyperemia**, **tuberculin**, **autoserotherapy**, or **Spengler's immunizing bodies**. Cramer and Bickel (Ann. de méd., Sept., 1922).

ENCEPHALOCELE.

This condition is also called *hernia* of the brain, or *hernia cerebri*.

The *congenital* form arises from failure of the walls of the cranial cavity properly to coalesce. It is usually seen at the posterior base, and is sometimes associated with spina bifida. The cerebellum especially is then involved. Other locations are the root of the nose, the frontal suture, or even within the nose or mouth. In some cases the protruding sac contains only cerebrospinal fluid, and it is then called a *meningocele*.

The *acquired* form has been seen after fracture or necrosis of the

skull. The commonest cause is the operation of trephining. The procedure known as a decompressive operation, which is done for the relief of pressure in cases, especially of brain tumor, is sometimes followed by a hernia of the brain. (See also FUNGUS, OR HERNIA, CEREBRI, p. 171, Vol. V).

The hernia is covered with the brain membranes and the scalp. These coverings may become very thin, and look as though they might rupture. Pulsation of the brain may sometimes be felt in the mass. Occasionally the tissues become inflamed, and even slough, requiring surgical interference.

The symptoms in some cases are only objective or even negative. In the congenital form, however, the condition is sometimes associated with other defects of development in the cerebrospinal axis. Pressure on the tumor in these cases causes temporary coma, paralysis, and other evidence of interference with the functions of the cerebrum.

The prognosis in congenital cases is bad, the patients seldom surviving more than a few years, or even months.

In the acquired form, especially after trephining, the symptoms are usually those that are due to the original lesion, such as trauma or tumor, rather than to the hernia itself. Cases vary greatly in this respect, however, and cannot be described here in detail. If the hernia should eventually lead to destruction of brain-tissue, especially in the motor region, corresponding symptoms would, of course, result.

VASCULAR DEGENERATION.

The blood-vessels of the brain, in common with those of the body gen-

erally, are subject to degenerative changes in their walls—the condition known as arteriosclerosis. The walls are thickened and become brittle, especially in advanced life. At the base of the brain, in the circle of Willis, and in the main trunks, these changes are often very marked. They are the causes of apoplexy, hemiplegia, aphasia, etc. The vessel either ruptures, causing a cerebral hemorrhage, or it is occluded by a thrombus, causing softening. (See CEREBRAL HEMORRHAGE, etc.)

Syphilis also causes thickening and degeneration of the blood-vessels. The inner coat is especially involved—the syphilitic endarteritis of Heubner. The resulting symptoms may be due to softening or hemorrhage, and are chiefly various forms of paralysis, as hemiplegia, monoplegia, aphasia, etc. (See also SYPHILIS and under the following heading: VASCULAR DISEASES OF THE BRAIN.)

JAMES HENDRIE LLOYD,
Philadelphia.

MENINGES AND BRAIN, DISEASES OF (CONTINUED).

VASCULAR DISEASES OF THE BRAIN.—The subjects of CEREBRAL HEMORRHAGE, ENCEPHALITIS, CEREBRAL ABSCESS, and HYDROCEPHALUS have been already treated, and hence need no further mention.

Cerebral vascular diseases might be considered as to their effects: 1. On the permeability of the vessel walls. 2. On the vasomotor arrangements for the brain itself. 3. On the brain tissue involved by vascular obstruction.

The main factor so far known regarding the vascular pathology of the brain hinges on the last one of these

points. Hence the best basis for approaching this subject is an outline of the effects produced by blocking of each individual vessel or branch. The causes and consequences will then admit of a more concise and satisfactory handling.

In general, it may be said that the effects are somewhat proportional to the size of the vessel and the suddenness with which the block occurs. Of course, as regards the eventual amount of anatomical damage suddenness has little to do.

GENERAL SYMPTOMATOLOGY.

Arteries.—(a) *The Dural Arteries.*—For two reasons, obstruction in these is harmless. In the first place, they do not have to do with the brain proper, but constitute in this particular an independent system. In the second, they are not terminal vessels, but are at all points protected by ample anastomoses.

(b) *The Brain Arteries Proper.*—The main factor here is the fact that, aside from the chief trunks, all the distributing vessels are more or less terminal arteries, and in part strictly so. Consequently the area supplied by any one of them is, in case of closure (embolism, thrombosis, obliterating arteritis, or enduring functional spasm), bound to undergo softening to a corresponding extent—the whole area, if a strictly terminal vessel, and a portion if only partially so.

The true terminal arteries are the perforants at the base and the small branches from the basilar directly entering the pons. But beyond the circle of Willis, all the pial arteries of much size are partially terminal.

The Individual Arteries and Branches.—*Lenticulostriate Artery*

(*One of the Preperforating from First Part of Sylvian*).—Partial softening in shape of a wedge with its tip in the interior part of the lenticular nucleus, while its base is directed forward and takes in the anterior two-thirds of the striate body. The wedge is formed of the anterior part of caudate, the internal capsule, and the third segment of the lenticular nucleus. Motor paralysis of the opposite side.

Lenticulo-optic Artery (also from Sylvian).—Softening of postexternal part of lenticular nucleus, of part of internal capsule, of anterior part of thalamus, and of tail of caudate.

Perforating Arteries from Choroid Plexus.—Partial softening of thalamus, size of a pea to a filbert.

Postexternal Optic Artery.—Walnut-sized softening in the subposterior part of thalamus and in the peduncle.

Precerebral plus Sylvian Artery.—Block at bifurcation of internal carotid, extending in the precerebral beyond the precommunicans. Softening of frontal, parietal, and sphenoid lobes, the striate body, etc.: i.e., of the whole territory supplied by both the precerebral and medicerebral arteries. Here we may have opposite hemiplegia, and, if on the side of the speech-centers, “total aphasia, together with an altogether unusual amount of mental degradation, in addition to blindness and loss of smell on the side of the lesion. The extra mental degradation would be due to the fact of the cutting off of the blood-supply from the callosum, seeing that this is mainly supplied from the precerebral.”

Precerebral Artery Alone.—Softening of the frontal convolutions and of the inner surface of the hemisphere as far as the callosomarginal fissure.

Branches of the Precerebral.—1. *Subfrontal Branches.*—Softening of orbital convolutions. No distinguishing symptoms.

2. *Interior Prefrontal Branches.*—Softening of the first and of much of second frontal convolutions. Likewise part of so-called "silent" regions of brain.

3. *Posterior Branches.*—Softening of remaining median surface of hemisphere supplied by precerebral artery. Crural monoplegia.

(A) *Medicerebral Artery* (in its first 2 cm., from which part are given off the preperforations above mentioned).—Softening of whole territory of Sylvian artery (same parts as in B); also motor segment of internal capsule, corpus striatum (thus including lenticular and caudate nuclei), and anterior third of thalamus. The symptomatology is also practically same as in B, except—if possible—more pronounced and with deeper mental impairment.

(B) *Sylvian Artery, Beyond the Perforations, or all its Branches.*—Total softening of cortical territory of Sylvian (*v. infra*: branches). Blocking here causes complete hemiplegia of opposite side (with exception of the trunk and other bilaterally acting muscles) and "total aphasia" if on the side of the speech centers; "that is, in addition to aphasia proper there would also be agraphia, as well as complete word-deafness and word-blindness, carrying with them that amount of mental degradation which is inseparable from a blotting out of all the word centers in the leading hemisphere." Astereognosis and early apraxia may be added.

Cortical Branches of Sylvian Artery.—The clinical results here vary some

according to the slight variation in different individuals in the extent of cortex supplied by this vessel, but even more upon the differences in the freedom of the anastomoses existing between its branches (cortical) and those of the precerebral and post-cerebral.

1. *Subfrontal Branch.*—Softening of part of insula and of the subfrontal (Broca's) convolution. Aphasia if on the left side, without other paralytic complications.

2. *Preparietal Branch.*—Softening of foot of medifrontal and part of precentral convolutions. Agraphia if on the left.

3. *Mediparietal Branch.*—Softening of both central convolutions along the Rolandic fissure, of the anterior portion of the first parietal convolution, and of the insula. In either of the last (Nos. 2 and 3) there may be aphasia due to cutting off of subcortical tracts, paralysis of face and arm on opposite side, and paresis of opposite lower extremity. Also paralytic agraphia, if on the left. Theoretically, according to Bastian, also loss of muscular sense in the fully paralyzed parts,—though impossible to demonstrate.

4 and 5. *Postparietal and Temporal Branches.*—Softening of the subparietal and supratemporal convolutions, and of part of the insula. Word-blindness and more or less complete word-deafness.

"It is only on rare occasions that vascular lesions are precisely limited to the seats of particular word-centers. They are much more frequently irregular in their distribution, or multiple, and thus give rise to confused or less typical forms of speech defect."

Postcerebral Artery.—More or less softening of the occipital lobe, especially the cortex on its inner and under aspects, including the region of the cuneus, the hippocampal gyrus, and posterior portion of lower temporal convolutions. Hemianopsia of the opposite half of the visual field, with preservation of pupillary reactions from both halves of the retina.

Cerebellar Arteries.—Embolitic and thrombotic softening here is more rare.

Vertebral Arteries.—Embolisms of the vertebral are more often on the left, due to the existence on that side of a marked constriction where the vessel discharges into the basilar, whereby emboli are caught at that point. Softening may not result. If, however, the block extends any distance along the artery (as is usually the case in thrombosis), softening in the corresponding half of the oblongata may be expected.

Basilar Artery.—Blocking of this vessel, usually thrombotic, so long as the postcommunicants are patent, only produces symptoms by cutting off the small terminal branches to the pons. These are, however, important, and two types of effect are distinguished according as the block affects the upper or lower portion. Where the focus is at the upper limits of the pons, involving cerebral crus, corpora quadrigemina, and optic tract, there may be a paralysis of the extremities on one side with that of the eye muscles on the other (hemiplegia alternans superior). Where, however, this affects the pons at the facial-nerve exit, there may be paralysis of the extremities on one side with that of the facial on the opposite side (hemiplegia alternans inferior).

EMBOLISM.

DEFINITION.—Embolism of the brain, like that in other parts of the body, is the blocking of an artery by a plug or material sufficiently solid to stop its blood-current. It plays a more important part here because: 1. The arteries are, to a greater extent than in most other parts, terminal vessels. 2. The special functions of any destroyed part of the brain cannot be compensated; as *e.g.*, in the lungs or spleen, where all portions act practically alike.

VARIETIES.—Transient Embolism.—In this form the occluding substance breaks up or is floated along to a place where the collaterals suffice, and this happens before death of the threatened tissues. It is believed to explain occasional transient seizures experienced by embolic subjects.

Simple Embolism.—The ordinary form, where the floating mass lodges in some artery and cuts off the whole current immediately.

Septic Embolism.—Where the embolic plug carries some infecting agent. Inasmuch as an ulcerative endocarditis may be due to the invasion of the ordinary pus-organisms (streptococci and staphylococci), gonococcus, tubercle bacilli, or even certain other micro-organisms, it follows that a plug carried to the brain may be the transporter of infection like that of its source. In such cases the reaction about the point of lodgment or in the involved area will bear some relation to the virulence of the underlying germ.

It is a notable fact that a septic cerebral embolism is far more liable than any other to form the starting-point of a hemorrhage. It seems to start from the eroded end of the vessel.

Aneurisms of the brain arteries in children are said to owe their origin to embolic processes.

Partial Embolism.—In such a case the plug, owing to its angular or irregular shape, does not at first completely block the vessel. Accordingly, either it is soon driven along to some point where it does fully occlude the lumen, or a thrombotic deposit soon forms around it and thus completes the closure.

Symmetrical Embolisms.—The corresponding vessels on the two sides have, in rare instances, been the seat of embolism (both medicerebrals, in Carrington's case; both the medicerebrals and precerebrals on each side in Eisendrath's).

Pigment and Granular Emboli.—The collections of pigment in chronic malaria are well known. Globular hyaline masses have been described by Manasse, and are supposed to be derived from the white corpuscles. So far as concerns chorea, however, clinical and experimental studies have disproved the theory that it is due to multiple small emboli.

Fat Embolism.—This affects primarily the lungs, but in general fat embolism the brain arteries may also be invaded. Only in severe cases are serious brain symptoms produced, and fever does not result.

Case of fat embolism of the brain in a robust young man who had both femurs broken in the caving in of a mine. There was little shock and he seemed to be doing well for twenty-four hours; then he became somnolent and succumbed in coma the third day. Autopsy revealed the cerebral form of fat embolism. The sufferer had dragged himself some distance from the scene of the accident to give the alarm for 4 buried mates. After any fracture all manipulation

and transportation of the injured should be reduced to the minimum, for fear of inducing fat embolism. It is better even to refrain from changing the dressings too often. The writer has known of instances in which the cerebral symptoms developed during or shortly after the patient had been moved. Weber (*Med. Klin.*, May 25, 1913).

Attention called to certain signs of value in the differentiation of fat embolism from traumatic intracranial hemorrhage. Absence of slow pulse and of abnormal pupillary conditions speaks for the former condition. There is no choked disk, and generally no headache nor vomiting. There are commonly fat droplets in the urine and numerous punctate skin hemorrhages. Melchior (*Mitt. a. d. Grenzg. d. Med. u. Chir.*, xxxviii, 178, 1924).

Case of air embolism occurring during urethroscopy. A man aged 60 had had difficulty in micturition, which had been relieved by passage of a blood-clot. A No. 10 coudé catheter was held up at the bulb and started slight bleeding at once. A Joly urethroscope was used and under air inflation the urethral wall in front of the bulb was seen to be covered with granulation tissue. The presence of some surgical emphysema of the penis was then noticed. In 3 minutes after the air had been pumped into the urethra, symptoms of air embolism set in. The patient was dazed and restless, gradually lost consciousness, and became cyanosed, with stertorous breathing. The respiration slowed and eventually ceased. The pulse later became impalpable, 8 minutes after the initial symptoms. Treatment consisted of injections of **strychnine** and **camphor**, with **oxygen** directed over the face. **Artificial respiration** was carried out for a few minutes, when the patient began to move his limbs and normal respiration was restored, followed by gradual return of consciousness. Most cases of air embolism have occurred in connection with operations on the lungs and air passages. R. S. Roper (*Lancet*, Jan. 17, 1925).

Air Embolism.—The same applies as to fat embolism. This refers only to cases where the air enters at other points in the body.

There is also the possibility of air entering through the brain vessels; but this applies not to the arteries, but to the veins and sinuses. In Genzmer's case air to a fatal extent was aspirated through the opened longitudinal sinus. François-Franck's experiments appear to show that by way of the vertebral veins air may be taken in through the occipital diploë veins. In the Porter case there was some evidence that air was introduced into brain-vessels in tetanic convulsions, the wound being across the forehead. Koerner concludes that in operations on the lateral sinus, where the sinus-wall shows respiratory movements, the vessel should first be closed below before venturing to open it, lest air be sucked in.

SYMPTOMS.—These are largely dropping out of functions (*ausfall symptome*) rather than strictly positive. They are, as a rule, though not invariably, those of a sudden interruption of function of the portion of the brain involved, sudden in onset and promptly complete in effect. Rarely they deepen for hours after the onset. They necessarily vary in intensity and kind according to the extent and location of the area supplied by the vessel. Certain immediate effects may pass off, and some of the more lasting manifestations may gradually ameliorate.

There are no focal premonitions (as headache, dizziness, unilateral tinglings or numbness about the body, paresis, etc.), and previous headaches, apparently in relation to the trouble, count against embolism.

Aphasia speaks in general more for embolism than for hemorrhage, though common enough in the latter also. Development of the condition during sleep makes the probabilities against embolism.

A history of past rheumatism, especially the presence of a heart murmur, and still more a knowledge of previous vascular plugging (in any part of the body) are strongly suggestive of embolism. To fully warrant the diagnosis, we must establish the existence of some source, as valvular disease or endocarditis at the time of the seizure, though various pulmonary and other conditions may suffice.

The occurrence of apoplexy or hemiplegia in persons under 40 years of age has been supposed to indicate embolism, though there are too many exceptions to allow much value to any such age rule.

The occurrence of coma argues against embolism; at least, embolism limited to the pallium is not attended by this symptom, and this is its most common location.

The focal symptoms are those of the part involved, and may include almost any loss of function seen in brain disease, though they are more often those of the left side of the brain. For the regional diagnosis (localization) these have been given in brief outline in the schedule of arteries.

ETIOLOGY.—This has been given in part under the heading VARIETIES.

The forms of verrucous and ulcerative endocarditis, yielding vegetations or other solid fragments that may become freed from their base, are the best-recognized causes of embolism. It has been found that embolism of the brain occurs in 5 per cent. of cases

of valvular disease, and that this occurs twice as frequently in females as in males.

Rheumatism, gonorrhea, chorea, scarlet fever, appendicitis, and septic processes of all kinds in whatever part of the body, by their tendency to endocarditis, are indirect causes of embolism. Destructive pulmonary processes, pleural irrigation, and enteroperitoneal troubles may free thrombi that find lodgment in the brain.

PATHOLOGY.—The main feature is the softening, and this involves all tissues so far as it goes. It may be red, white, gray, yellow, or brownish, dependent on circumstances, duration, etc. "In the early stages of embolism or thrombosis of vessels supplying the cortex, red or red and white softening mixed is found in the area affected; after longer periods yellow softening is met with, or what French writers term *plaques jaunes*, and, after much more prolonged periods, pseudocysts are found, owing to complete atrophy and absorption of the cerebral tissue."

It is still an open question whether all focal softening of this type is due to vascular blocking. If so, then in numerous cases either the obstructing material has disappeared or the trouble has been an arterial spasm of sufficient severity and duration to produce the same effect. The left side, and especially the left Sylvian and its branches, is the more frequent site.

PROGNOSIS.—Experience shows that the prospect of late improvement after embolism is as good as after cerebral hemorrhage. In favorable locations a certain amount of collateral compensation occurs, so that a marginal zone of endangered tissue

recovers a sufficient degree of supply to resume function. Moreover, many of these are young subjects in whom some substitution of function is still possible. Immediate danger to life occurs only when the area involved is great, or where essential centers in the pons are included.

TREATMENT.—The treatment of this condition is in some respects different from that for cerebral hemorrhage. The patient should **rest in bed** with the **head low** and the body in the fully reclining position, in order to favor the cerebral circulation. Where there is a tendency to shock, with weak heart action and low blood-pressure, circulatory stimulation with such agents as **aromatic spirits of ammonia**, **ammonium carbonate**, **ether** and **camphor hypodermically**, **alcoholic preparations**, **strychnine** and **caffeine** is indicated, and **external heat** should be applied.

Increased circulation in the depleted brain area may probably be promoted by the repeated administration of **nitroglycerin** or **amyl nitrite**, acting as vasodilators.

Where the block is due to atheromatous or other soft material, it may break up sufficiently to pass on, and artificial activation of the circulation, with a rise of blood-pressure, might be expected to be of assistance by forcing the embolus as far as possible from the larger trunk into the more peripheral vessels. Yet it should be remembered that unusual circulatory activity will often involve the risk of tearing off further emboli.

Venesection and purgation are contraindicated in these cases, and the **ice-bag** to the head should be applied only if symptoms of irritation later appear.

The management of the case after the embolic softening has fully developed is that of hemiplegics in general. We may not remove the focus, but we can look after the general health and do much, by training the patient, to regain full power of what is left. Administration of **potassium iodide** is advisable, especially if there is evidence of syphilitic arteritis.

THROMBOSIS.

DEFINITION.—Under this general heading it is convenient to include the blocking due to specific autochthonic coagulation, arterial disease, obliterating endarteritis, etc. To some extent these are distinguishable conditions clinically and therapeutically, yet they have much in common. In this sense it includes all cases where local processes or disease conditions lead to vascular occlusion and thus to the production of symptoms, if any are present. While there may be a wide difference in the origin of these cases, the final stroke usually depends on a local coagulation or deposit of material from the blood. If the vessel be previously narrowed, then, of course, much less will suffice to block it.

VARIETIES.—There is, in the first place, a wide distinction between arterial and venous thrombosis.

Arterial.—This presents several subforms:—

1. One is due to conditions of the blood favoring the formation of clot (leucocytosis, increase of coagulation ferment), as in chlorosis and the puerperium; or to a thickening of the blood and slowing of its current, as in certain diseases attended by debility and exhaustion.

2. Due to trauma, ligature (as in Marchand's case, where fatal throm-

bosis of the Sylvian artery extended up from a ligation of the carotid), adjacent inflammations, and encroachments or compression, as by neoplasm. The traumatic cause may be either operative or accidental. According to Gerhardt, thrombosis in the branches of the Sylvian artery may occur in tuberculous meningitis and thus account for the hemiplegic symptoms in some of those cases.

Otherwise this form is so rare as to merit merely enumeration. The causes of both Form 1 and Form 2 act even more frequently to produce sinus thrombosis.

3. That due to syphilitic arteritis. Here the progressive narrowing of the arterial lumen at length reaches such a degree as either to cut off directly the blood-current or to slow it so that coagulation occurs.

4. The atheromatous and allied changes in the arterial wall found in the aged, acting in much the same way as the specific form. Arteriosclerosis with or without nephritis might be supposed to favor thrombosis, but the accompanying increase in blood-pressure serves largely to prevent this; hemorrhage is the far more frequent result. Gout and rheumatism are favoring antecedents.

SYMPTOMS.—In general, these are gradual in onset and for a time progressive in character. In contrast to this is the fact that there are no prodromata in embolism and at least much less tendency to them in hemorrhage. The age, general condition, and personal history of the patient are all-important aids in the diagnosis.

Loss of consciousness is not the rule in thrombosis, or not until the condition is so far advanced as to approach a fatal ending. There is a

tendency to a slowing of the pulse. It may, however, vary considerably from time to time, and may increase, of course, if there is any complicating sepsis. This slowing occurs, no matter what part of the brain is especially involved, though, doubtless, it is more pronounced when the basilar is the seat,—and there is a possibility that in all cases where present it is due to participation of that vessel.

Fever is not an accompaniment of the thrombotic process in itself, and occurs only secondary to some outside inflammation or to septic disintegration of the thrombus itself. Barring sepsis, there is, on the contrary, an inclination to subnormal temperature, though this feature will take an irregular course. "Yawning, and especially sighing, at times in respiration are frequent and noticeable symptoms in thrombosis and its precedent conditions, though also common in advanced cerebral hemorrhage." Apoplectic motation, so common in progressing brain hemorrhage, is here absent.

The fact that compression of the carotids may aggravate existing symptoms and even bring on slight convulsions in persons suffering from impairment of the brain circulation, especially thrombotic plugging of the basilar (Griesinger's syndrome), has suggested it as an expedient in the diagnosis of thrombosis. But as it affects disadvantageously the patient's cerebral condition, and possibly involves injury to an old person's carotids, it is generally discountenanced.

Occasionally, in persons of some intellectuality, it is quite possible to locate the trouble in the field of one or more arteries, preferably the Syl-

vian or its branches (for which purpose compare the schedule of arteries above given).

In the autochthonic form (due to overcoagulability of the blood, retardation of the current, etc.) there may be no distinct forerunners, but only a progressive increase in symptoms and severity. This developmental stage may be very short if the process is limited to a single vessel, or may steadily increase to a fatal termination if it extends to other vessels, for the conditions which started the process may continue to extend it. "Aphasic and amnesic defects of speech have been met with occasionally during or after acute specific diseases, or during the puerperal state, and in all such cases a thrombosis, partial or complete, of the left cerebral artery is the most common cause" (Gerhardt), though the same causes may favor embolism.

In the other two chief forms we have a history of past syphilis, the evidence of advanced arteriosclerosis, or a senile subject usually advanced in years to give us a distinct clue. Here prolonged and wavering prodromata, especially if diffuse or scattering and not focal, strongly suggest thrombosis. There are frequently such warnings and forerunners of various kinds. Transitory paresthesiæ (tinglings, numbness, etc.), pareses, aphasic spells, twitchings, headaches, visual obscurations, cardiac and respiratory irregularities, lapses of memory, mental hebetude, dizziness, etc., according to the location and extent of the threatened area, are more or less frequent. If unilateral in type, they are the more in evidence. These, at times, last over a period of weeks or months, but

often are of a few days' or less duration. "The physiologically recurring waves of vessel contraction and diurnal or other periods of fall in blood-pressure, added to the pathological narrowing of the vessel (where there is danger of thrombosis), may evidently, for a time, limit the nourishment of the respective area sufficiently to impair its function without actually causing necrosis. The tissues are still supplied with enough to keep them alive, and as soon as the flow again increases these resume their functions. Presently, however, if relief is not obtained, the matter goes too far, and irreparable softening ensues." In some of these cases conditions of *astasia-abasia*, *dyslexia*, etc., are noticeable. In reading, writing, muscular or other effort there is a quick tiring of function. "The centers act normally for a brief period, then fag out." This may apply to large areas or almost the whole brain; it is more often one-sided or even further limited.

Some authorities claim that the specific form is usually limited to a single vessel or a few branches, and hence is focal in character, but to this there are certainly many exceptions. In the senile type, however, the process is widely distributed, and hence the manifestations are more general and diffuse. This applies more especially to the prodromata and general features than to the symptoms following the softening,—which latter necessarily represents one or more distinct foci.

"In the specific form, which may occur at almost any period of life, there may, or oftener may not, be much headache; if especially nocturnal, so much the more in evi-

dence." Ophthalmologists recognize a *chorioretinitis syphilitica* as analogous to specific diseases of the brain arteries. In suspected cases lacking a definite history of syphilis a careful search must be made for any marks about the body or other indications pointing or not to that diagnosis; Wassermann tests, or an excess of leucocytes in the spinal fluid, may give confirmation.

ETIOLOGY.—Certain general influences play a secondary rôle. All debilitating and wasting diseases, by weakening the circulatory force and by reduction of the traversing fluid, have such a tendency. Excessively warm weather, a rapid rise in the atmospheric temperature, and marked fall of the barometric pressure favor the occurrence of thrombosis, while opposed to cerebral hemorrhage. Senility also acts in the same sense, as well as in a more direct manner.

The more immediate causes fall under two heads:—

1. Local disease of the vessel walls. Atheroma, pre-eminently a disease of the old and favored by chronic alcoholism, occupies a prominent place here. It narrows the lumen of the vessel, but may also be the object around which the thrombus starts. Syphilis acts essentially by thickening of the arterial wall (*endarteritis syphilitica*, *periarteritis nodosa*, etc.); it is said to cause thrombosis chiefly in those between 20 and 50 years of age.

Sometimes the thrombosis starts in an aneurismatically dilated artery.

2. It may be due to a strong tendency of the blood to clot (*leucocytosis* often present). This is a much less frequent cause. Gout, chlorosis, and especially the *puerperium* (when the

vessels of the uterus have to be closed by clot) here play a rôle. In such case a practically spontaneous coagulation occurs and obstructs an otherwise healthy vessel.

PATHOLOGY.—This is, from a practical standpoint, simple, and corresponds closely to that of embolism. Inasmuch, however, as the remaining vessels are so often more or less similarly diseased in the common forms, the chances of establishing an adequate collateral circulation are not as favorable. Consequently the area of softening, for any given vessel, is rather larger. So soon as the current has been entirely cut off for a short time, a few hours or probably less, necrosis is established and the part thus affected is hopelessly lost. The later course of such a focus is the same as that after embolism.

PROGNOSIS.—This has reference to three points:—

1. The prodromal stage. Where it is possible to make the diagnosis and institute treatment at this stage, softening can usually be headed off. This is quite intelligible in syphilis, though there is a great tendency to recurrence. And even if the specific process is absorbed, there remains ever after a weak spot in the arterial parietes that may under strain give way and be the source of a hemorrhage. The senile gouty and atheromatous forms are also amenable, and not infrequently seem to recover permanently. Of course, in that happy event it is not to be supposed that the artery wall is rejuvenated, but only that things have so adjusted themselves that there are no longer active manifestations.

2. The thrombotic softening. This in itself is, as above stated, somewhat

less favorable than in embolism. The tissue loss is permanent, and function can be compensated only to a degree.

3. The tendency of the process to extend. It is difficult to be very explicit on this point. In many cases there is reason to think that numerous vessels are more or less affected by the same process and that the same dyscrasic cause continues, only that it reaches extremes in but one or two at a time. Unless very carefully managed, we may expect that, sooner or later the danger limit will be reached in some of these.

TREATMENT.—To be successful this must be prophylactic and directed to the prodromal stage. The trouble is of slower development than hemorrhage or embolism, and needs be met with less vigor, but more persistence and greater skill in adaptation of means to an end. There is one danger in the measures for relief: we are dealing with diseased vessels, their walls being often much weakened; there is no such disturbing fear in embolism, for there the vessels are presumably healthy; nor in hemorrhage, for there our efforts at relief involve no strain on the vessels.

When we find signs of such danger impending, the first or immediate line of treatment is analogous to that in embolism (*q.v.*). Circulatory weakness, if present, calls for **strychnine** and other stimulating agents. The **nitrites** may be used for the purpose of relaxing the affected vessels. In this connection the slowly, continuously acting nitrites are the most desirable. In the practical use of the nitrites, however, there is one point not duly appreciated. From **nitroglycerin** we rarely get any stomach

disturbance; but from **sodium nitrite** and, though less, also from **erythrol tetranitrate** there is very often complaint of much discomfort about the region of the stomach, and it is the same in whatever way administered. The objection to these latter remedies is time and again so great that they have to be discontinued. Still, even then we can fall back on the **nitro-glycerin** and succeed fairly well. **Alcoholic stimulants in small amounts and diluted** give valuable temporary aid, when not otherwise contra-indicated.

To reduce the coagulability of the blood, **citric acid**, given as lemon juice in plenty of water, may be tried.

As soon as immediate relief is secured a course must be adopted looking to more lasting benefit.

For arteriosclerosis small, long-continued doses of **iodide of potassium** are much used. The non-saccharated, dilute solution of **hydriodic acid** is usually more satisfactory; 5 to 10 drops, well diluted and after meals, can be given for considerable periods and tend less to iodism.

Since most of the aged patients show a rheumatic or gouty tendency, wastes not being eliminated with due promptness and causing or aggravating the arteriosclerotic trouble, **alkalies and salines** are frequently indicated. Much aid, moreover, is furnished by certain of the **sulphur waters**. If it is possible for the patient to visit the springs, so much the better; otherwise the waters may be employed at home. A course of these waters can be repeated from time to time.

Report of 2 cases with foci of softening in the brain, apparently the result

of a puerperal cerebral thrombosis preceded by pelvic or femoral phlebitis. In the first case there resulted progressive hemiplegia 50 days after delivery, developing insidiously without ictus, and gradually retrogressing almost entirely in a few months. In the second case facial hemiparesis with aphasia and transient mental impairment developed gradually the eighteenth day after delivery. After 4 months there was marked betterment. Crémieu and Gauthier (*Prog. méd.*, Mar. 5, 1921).

In the syphilitic form the whole power of our therapeutic resources should be promptly brought to bear and continued until all symptoms are well in hand. It should be borne in mind that often the so-called specifics will develop this desired local action only after the vessels have been dilated. So long as they are almost closed, it is evident that little blood, and consequently little of the medication, can reach the imperiled point.

THROMBOSIS OF THE BRAIN VEINS AND SINUSES.

Veins.—Primary thrombosis of brain veins has been but rarely observed. Hence, despite the occasional description of cases in the literature, it is impossible to present anything very systematic in regard to the matter.

Without doubt it is of greater frequency than appears from the above. The reason why it is not more recognized is that in itself it but very exceptionally causes symptoms. All the pial veins have numerous and free anastomoses, so that serious stasis only results when whole networks of contiguous veins are filled. In the latter event softening of the corresponding drainage area has been noted. In such a case a focal diagnosis is the most that one might ex-

pect to make. If other manifestations are present, they are usually due, as in sinus trouble, to sepsis rather than the thrombosis as such.

The question of terminal veins in the brain is not fully decided, though only as regards the perforatings, the prefrontal efferents, and parts of the internal or Galen's system: the same parts, it may be remarked, where the arteries are strictly terminal. The balance of evidence favors the view that in these limited sections there are at least many connections between the finer branches.

More often there is a secondary venous thrombosis here, an extension backward of a like process in the sinus into which the vein empties.

Cretefaction and fatty degeneration of the parietes of these vessels also occur, though, of course, without clinical significance, and the same applies to the endophlebitis deformans chronica described by Huber.

Sinus Thrombosis.—This is a blocking of any one or more of the several venous sinuses of the brain.

Such obstruction is, of course, never of embolic origin, but always due to thrombosis (or, in rare cases, to trauma or ligature). Neighboring septic trouble is more often a cause than in the case of the arteries, but otherwise disease of the vascular wall plays no such part as with the arteries. The causes are, however, many. In children it occurs in marasmus, cholera infantum, whooping-cough, and other conditions of extreme exhaustion. In the adult, chlorosis, pregnancy and the puerperium, erysipelas (by extension, centrally, of a process starting at the surface), cholera and like disorders that greatly reduce the body fluids, sep-

tic processes in adjacent tissues, and any form of debility that greatly weakens the circulation. Most frequent of all are the cases of phlebitis of the lateral, petrosal, and connecting sinuses, due to extension of inflammation from ear disease (see HEAD AND BRAIN, SURGICAL DISEASES OF: INFECTIVE SINUS THROMBOSIS, Vol. V).

There are other less frequent forms of inflammation, starting, perhaps, in the parasinoidal spaces and involving the sinuses.

SYMPTOMS.—It should be remembered that one or both jugulars may be tied, one or even both lateral sinuses closed, or almost any single sinus blocked, without the necessary production of symptoms, as has been many times shown by clinical, operative, and, in animals, experimental evidence. The only exception to this is the straight and possibly the two cavernous sinuses. In the very young, the feeble, or those otherwise exhausted, blocking of a sinus may have more effect, and be a factor in a general breakup.

The sinuses that are easy of access surgically are the longitudinal and the two laterals. Besides these, if warrantable, it would be quite possible to tie the end of the straight sinus.

Thrombosis of the brain does not lead to any definite increase of the cerebrospinal fluid, as a rule. The only exception is where the outflow through the straight sinus is interfered with, or, possibly, the venous discharge from the small fringe of choroid plexus in the angles of the fourth ventricle.

For the most part, the symptoms attributed to sinus thrombosis are really due to the attendant sepsis or an exten-

sion of the inflammation to neighboring structures. Consequently it is only incumbent here to consider the cases where positive symptoms are due to the blocking as such.

It has been claimed by Voss that a murmur can be detected in the unobstructed internal jugular vein, or that it can be produced artificially by a slight pressure of the stethoscope on the neck close to the base of the skull. If, however, the murmur is absent despite such reinforcement, while present on the other side, there must be occlusion of the sinus.

The presence or absence of a sinus pulse has no diagnostic value as regards thrombosis.

In lateral sinus thrombosis a profuse aural discharge may greatly diminish or even cease. The pain ranges from slight to excruciating, and may radiate over any part of the head or neck. Positive blood cultures are accepted by some as wholly characteristic; but sepsis does occur in their absence, or the occluding clot may be sterile. Cultures are useful where other sources of infection can be eliminated, and, where the clinical symptoms alone are not distinctive. Rigors in either acute or chronic tympanic suppuration are almost pathognomonic, especially if optic neuritis is present. Dilatation of the superficial veins of the temples, forehead and eyelids follows pressure on a normal jugular, but not on an obstructed jugular. Palpation of the jugular for a cord-like mass may be misleading. Exploration is indicated by repeated chills, a rapid rise of temperature, irregular in type, increased pulse rate followed by sweating, and a high polymorphonuclear percentage and leukocyte count. Diagnostic puncture of the sinus is still in vogue, chiefly because it is less dangerous than incision, but is not always definitely informative, since in parietal thrombus the circulation is

still present. When knowledge gained from puncture is insufficient, incision must always be employed. X-ray findings are of little diagnostic value. Vomiting is not infrequent, but not characteristic. Mental clarity is a very important symptom. Lumbar puncture offers some help in differentiating meningitis from sinus thrombosis. S. MacCuen Smith (*Atlantic Med. Jour.*, June, 1924).

In cases of closure of the **sinus rectus**, **Galen's vein**, or the **velar veins**, there are three possible outcomes:—

1. Full physiological compensation. There appears to be no evidence that perfect compensation can occur.

2. An increase of ventricular fluid, leading to hydrocephalus.

The ample anastomoses described, and the fact that normally this venous current has to turn several sharp angles before leaving the skull, make it, at first, unintelligible why there should ever be any trouble following the closure of the sinus rectus or its practical extension, the single trunk of Galen's vein. And, *so far as concerns either the vitality of the tissues or the function of the brain substance and nerve substance proper, there is nothing to show that compensation is less perfect than where other brain veins are closed.*

The difference depends entirely on the presence, in the territory of this vein, of a peculiar structure, the choroidal tissue, occurring only in the brain ventricles. This tissue normally produces ventricular fluid. Its activity is easily influenced by many conditions, and it responds to any interference with the venous discharge by increased production of fluid.

It is, then, not primarily any venous stasis that causes symptoms, but only the secondary hydrocephalus. And the facts show that this

is always bound to occur. This causes death, if at all, only after a lengthy period and in this indirect manner.

3. Early death.

If, however, the velars be closed (*i.e.*, the venae intimae be cut off from both their regular and collateral outlets), then, so far as present evidence goes, a speedy fatal ending is inevitable. This takes place before there is time for the development of much hydrocephalus, a small quantity of blood-tinged fluid being all that has accumulated.

It is still possible that if only the main trunk of one or both velars was obstructed, and the thrombus did not extend into any of their branches, the fatal ending might be delayed, but hardly for long.

Cavernous Sinuses.—In some cases simple blocking of a cavernous sinus may not cause marked symptoms. It depends upon how much of a *confluent* it happens to be in the individual case. Even when it receives a large basilar and a deep Sylvian branch, it is probable that other venous channels can re-establish an outlet and softening be avoided. The most definite symptoms are on the orbital side. There may be puffiness about the orbit, some distention of the veins in the same region, and even prominence of that eyeball or more lasting interference with the vision and nutrition of that eye. All such manifestations are more marked in septic than simple thrombosis. In the septic type, indeed, pronounced exophthalmos is characteristic, with edema of the lids, face, root of the nose and conjunctiva, and often ptosis, strabismus and finally complete fixity of the eyeball, due to implication of the 3d, 4th and 6th cranial nerves. Early or pro-

dromal symptoms may be headache, with or without fever, pain in and around the eyes and in the teeth, diplopia and "cold in the head" (De Schweinitz). In a majority of the cases, the opposite side becomes involved 30 to 48 hours later, and recovery is rare.

TREATMENT.—Where the thrombus is of septic origin or has become infected, **surgical treatment** is called for. There is no safety or recovery until the material is removed. In simple or uncomplicated thrombosis, on the other hand, direct interference is not called for; prophylaxis, if anything, is the *desideratum*.

Eight **blood transfusions** by the syringe method, used in a case of sinus thrombosis resulting from ear infection, held the patient over repeated crises, bringing recovery in spite of complications in the pleura and joints. H. Koplik (Med. Rec., Jan. 3, 1920).

Of 5 cases of cavernous sinus thrombosis, one secondary to lateral sinus thrombosis and 4 to ethmoidal and sphenoidal sinus infection, only the first recovered—but with loss of sight in both eyes—following operation on the lateral sinus. In 2 of the others operative drainage was attempted after exposing the frontal lobe through the frontal sinus and bone and removing fluid by lumbar puncture, but without success. E. W. Day (Atlantic Med. Jour., June, 1924)

WILLIAM BROWNING,
Brooklyn.

MENINGITIS, CEREBROSPINAL.—The first authentic report of this disease in America dates back to 1806, and was made in Massachusetts. Judging from the record of mortality, no epidemic has been of so severe a type as that of 1905-06 in New York City.

Cerebrospinal meningitis was epidemic in New York in 1871-72. The

fulminating type predominated, and existed among the negroes. This epidemic continued until 1874, when it spread throughout the United States. In 1876 the disease appeared sporadically, and remained so until 1893, when a severe epidemic occurred. The disease again remained in its sporadic type until the severe epidemic of 1905-07. Since that time sporadic cases have appeared during the fall, winter, and spring months of the year.

A peculiar feature of this disease is that but a small proportion of the population is infected. When physicians and nurses are directly exposed they rarely contract the disease. During the four large epidemics in New York City the morbidity was as follows:—

1872	8.07 per 10,000
1881	3.70 per 10,000
1893	2.67 per 10,000
1904-05	6.30 per 10,000

Flügge estimated that during an epidemic fully 70 per cent. of the people living adjacent to meningitis patients are *carriers* of the meningococcus. These carriers have this pathogenic bacterium in the nasopharynx.

The disease was prevalent during the cool months in the camps of all the fighting nations. The carrier rate was carefully studied by the English in the civil and military population in both the endemic and epidemic forms. Two to 5 per cent. were found infected where the disease was endemic. In one garrison the carrier rate increasing as winter approached until it reached an extraordinary height in December. A rapid succession of cases tended to increase the virulence of the meningococci. To check the spread of the disease: 1. The individual soldiers were protected as

far as possible from infection by suitable ventilation and floor space, the elimination of carriers detected by cultures, and cleanliness both in the individuals and their surroundings. 2. Prophylactic injection of meningococci killed by a low heat or suitable antiseptic was used experimentally both in animals and man with apparently favorable results. Only a serum known to be polyvalent was used for treatment. 3. Disinfection of carriers was attempted on a very large scale with considerable success. The best results were obtained where the carriers entered rooms filled with a very fine spray. Zinc sulphate in 1 per cent. solution and chloramine-T in a 1 or 2 per cent. solution had given the best results. Anterior and posterior nasal sprays had also been used with some success. W. H. Park (Trans. Assoc. Greater N. Y.; N. Y. Med. Jour., Nov. 2, 1918).

In 1905, 2775 cases were reported to the New York Board of Health. Sixty-seven per cent. of these cases occurred in children under 10 years of age, and 15 per cent. in infants under 1 year of age. While a large number of cerebrospinal meningitis cases are reported to the Board of Health very many cases of a milder or abortive type were not reported. Registration of cases not being compulsory, frequently cases were reported as simple spinal meningitis or tuberculous meningitis which may or may not have been abnormal types of cerebrospinal meningitis.

In 1906, at the height of the epidemic, there were reported 1032 cases, with 812 deaths, in greater New York. In 1907 there were 828 cases reported, with 624 deaths. Thus, the mortality in 1906 was 78.7 per cent., and in 1907, 77.5 per cent. During the six months of 1908 there were reported 253 cases, with 182 deaths, the mortality being thus 71.9

per cent. Therefore, it may be stated that the mortality averages between 70 and 80 per cent.

During the great war, the year 1915 seems to have been a record one for this affection in France and England. In the zone of war activities in France the number of cases was 1073 and in England the incidence was 2566. Less than half the English cases occurred in soldiers. (Pathologia, cited by Med. Rec., Jan. 11, 1919).

SYMPTOMS.—During the epidemic in New York 3 classes of cases occurred—mild, abortive, and severe.

Mild Type.—Slight fever, generally malaise, and perhaps vomiting.

Abortive Type.—This type is usually seen in strong children, who are able to withstand a severe infection. By reason of their health they are less severely infected, as shown by their relatively mild symptoms and the rapidity of their convalescence.

The sporadic cases are often so mild, according to Koplik, that the intermittent or remittent febrile symptoms, headache and drowsiness, are the only ones that lead to a thought of cerebrospinal fever. The rigidity, hyperesthesia, Kernig sign, herpes, delirium, and gradually increasing hydrocephalus, as evidenced by the so-called Macewen sign, are usually present, but one rarely encounters the severer symptoms—sudden and abrupt unconsciousness, petechiæ or diffuse hemorrhages, and paralysis.

Case in which the patient complained merely of a persistent headache. Fever, vomiting, Kernig's sign, and neck pains were all lacking. The patient was comfortable aside from the headache and did not want to stay in bed. Lumbar puncture showed slightly increased pressure and diplococci morphologically similar to the meningococcus. Comporti (Rif. med., Nov. 6, 1922).

The onset is usually sudden, and I have seen meningeal symptoms subside within ten days with no

sequelæ. This happened in the case of a child with undoubted cerebrospinal meningitis in which the diagnosis was confirmed by bacteriological examination of the spinal fluid. Rhinitis with catarrhal discharge from the nose is sometimes an early symptom in this disorder; it is frequently found in the abortive type of the disease. The danger attending the presence of the meningococcus in the nose consists in the ease with which this pathogenic bacterium can enter the frontal sinus and thus give rise to encephalitis. Rimbaud noted epistaxis in 4 out of 12 cases, improvement apparently coinciding with the appearance of the symptom.

In the abortive type of the disease there frequently is a nasal discharge in which the *Meningococcus intracellularis* can be found long after the rhinitis has disappeared. The ambulatory cases are the ones which disseminate this infection, because they carry the pathogenic bacteria from house to house.

The writer saw cases in which the puncture fluid showed merely lymphocytosis and the disease progressed with extreme cachexia. In one case all the signs pointed to tuberculous meningitis until it was too late for serum treatment to be effectual. He emphasizes the need of repeated punctures for diagnosis. A meningococcal disorder should be suspected when several days of apyrexia are interrupted by periods of high fever and there is loss of weight. Bolaffi (Policlin., Feb., 1920).

Description of an "aseptic," sporadic form of acute meningitis. The symptoms are typical of epidemic meningitis, but the prognosis is favorable, the disorder lasting but a few days. Lymphocytes are found in the cerebrospinal fluid, which is sterile. Wallgren (Wien. Arch. f. inn. Med., Feb. 10, 1926).

Severe Type.—In the severe type there is a sudden onset of symptoms. In older children a distinct chill is usually the first symptom noted. The skin feels hot. The temperature rises to anywhere between 102° and 105° F. (38.8° and 40.6° C.) in the rectum.

The writer observed a case in which the temperature by rectum registered 109° F. (42.7° C.) by 3 different thermometers. A lumbar puncture brought a few drops of a turbid spinal fluid. Fifteen c.c. of **Flexner's serum** was given. Four hours later the temperature was 103.4° F. (39.6° C.). The patient, a baby, recovered. Manning (N. W. Med., Oct., 1920).

The pulse may be slow or rapid; the respiration irregular, sometimes sighing and labored, but most frequently Cheyne-Stokes in character. Later, there are vomiting, pain in the head,—in the frontal or occipital regions,—and pain at the back of the neck. There are moaning and frequently delirium. Vasomotor disturbances, such as the flushing of one ear or one cheek, are occasionally seen. The *tachic cérébrale* is usually noted upon stroking the breast with the finger-nail, a distinct hyperemia following, which remains for several minutes.

The tendons are very sensitive to the slightest pressure. The patellar reflexes are usually absent. When the thigh is flexed on the abdomen and we try to extend the leg there is considerable latent contraction,—the so-called *Kernig sign*. This symptom alone should not be depended upon. Hyperextension of the great toe produced by stroking the sole of the foot—the so-called *Babinski reflex*—is not always present; it is fre-

quently noted in perfectly healthy children. In a series of 50 children I examined, the Babinski reflex was found in 40.

Brudzinski's neck sign in tuberculous and other types of meningitis is present in 100 per cent. of those ill with either cerebrospinal meningitis or pneumococcal meningitis. The technique in eliciting the neck sign is as follows: The head is forcibly flexed with the left hand while the child is lying flat on its back; with the right hand pressure is meanwhile exerted on the chest to keep the child from being lifted. If the sign be positive, both legs will flex on the thighs and the thighs on the abdomen. The identical "collateral sign" consists in flexing the leg on the thigh and the thigh on the abdomen, when if the sign be positive the opposite lower member will assume the same position.

According to Parmele neck rigidity was practically universal in the 230 cases treated at the Kansas City General Hospital in 1912.

At the General Hospital No. 6, Fort McPherson, Ga., in the winter of 1917 and 1918, the cases showed no uniformity of symptoms or signs. The most uniform, however, were headache, 100 per cent.; fever, 80 per cent.; delirium, 60 per cent.; vomiting 60 per cent.; Kernig, 50 per cent.; opisthotonos, 30 per cent.; orthotonos, 20 per cent. No cases presented the hemorrhagic spinal spotted rash, but possibly the early administration of serum prevented it. Early diagnosis is often possible only by lumbar puncture, especially in cases of fever and delirium with no other physical signs. Camac and Bowman (Arch. Int. Med., Jan., 1919).

In normal cytology of the cerebrospinal fluid the number of lympho-

cytes varies from 0 to about 7 per cubic millimeter. In any meningeal irritation, acute or chronic, the lymphocytes increase in number; they may do so indefinitely, up to thousands per cubic millimeter. Examining a number of cerebrospinal fluids from infants, Kaplan found that in the tuberculous forms the lymphocytes predominate. In the other acute meningitides of children the polynuclears and lymphocytes were equal or nearly equal in number.

It is marvelous how readily the polynuclears diminish if a patient shows the slightest tendency to improve, and how, on the contrary, they increase as the inflammatory process grows worse. *Pari passu* with the polynuclear increase the Fehling reaction disappears. This point is extremely important, as there are a number of cases of tuberculous meningitis in which the tubercle bacillus cannot be found even if the antiformin or the Jousset method be used. In these instances the copper-reducing substance in the cerebrospinal fluid is considered as highly suggestive of the tuberculous nature of the meningitis. Non-reduction of the Fehling solution, or the appearance of a violet color change instead, is significant, in Kaplan's opinion, of the non-tuberculous nature of the affection, unless a mixed infection exists. In case a double infection is demonstrated microscopically the invader that has the upper hand in the infection is usually reflected in the behavior of the cerebrospinal fluid with the Fehling solution. If it be the tubercle bacillus, reduction will occur; if it be another organism, it will not. The latter occurrence is due

to the fact that the organism has produced a marked increase in the polynuclears, which are in some way responsible for non-reduction. The importance of cerebrospinal fluid examinations in pediatrics needs no emphasis.

Either constipation or diarrhea may be present. The bladder acts well, although enuresis may exist. In some cases there is a marked retention of urine.

Contrary to conditions observed in other infections, the urine is clear and abundant, with an exaggeration of the elimination of nitrogen and phosphates at the height of the disease. The subsidence of the temperature under the influence of the serum does not always mean that the disease is conquered; the proportion of nitrogen in the urine may remain high, showing that the disease still has the upper hand, and that it is necessary to keep up the serum until the amount of urea in the urine begins to decline. Galebert and Thubert (*Revue de méd.*, March, 1910).

The joints are usually swollen, simulating rheumatism in such cases. There is also a distinct petechial eruption in some cases. In a series of 22 cases seen by me 6 showed distinct petechiæ; in 6 others the skin showed a distinct eruption resembling that of scarlet fever. Owing to the spots present in this condition, the disease was frequently termed "spotted fever." The pupils are usually dilated; sometimes they are irregular. I have seen cases—during the epidemic of 1905—in which one pupil showed marked dilatation, while the other was contracted almost to pinpoint size. Strabismus is a frequent symptom. Occasionally one notes nystagmus. Photophobia is common; in one of my cases the

child cried whenever a lighted candle was brought near the eyes. Opisthotonos is usually present. The severe rigidity of the sternocleidomastoid muscle, added to the marked rigidity of the arms and legs, forms a very prominent symptom during the course of the disease. Owing to these severe contractures, one usually notes constant moaning, very probably induced by the pain occasioned thereby.

Macewen's sign is elicited by percussion over the lower frontal bone or squamous portion of the parietal with the patient in the sitting posture and with the head inclined to one side. A hollow, resonant or tympanitic note is an indication of internal hydrocephalus. This sign is not always present and should not be depended upon independently for diagnosis, Koplik having found it present also in 34 out of 52 cases of tuberculous meningitis.

According to Burvill-Holmes, analgesia, or partial or complete anesthesia of the conjunctiva and cornea may be elicited in about $\frac{1}{2}$ the cases of cerebrospinal meningitis, even in patients who are perfectly conscious.

The writer has observed an erythematous rash very early after the onset, and before there were any symptoms of meningitis to suggest the diagnosis. In one case there was a profuse rash to be seen 6 hours after the onset, disappearing 4 hours later. In the second case the rash was present 12 hours after onset and had almost disappeared 6 hours later. Symonds (*Lancet*, July 21, 1917).

The *toe sign* is an early evidence of meningitis. Flexion of the completely extended leg at the hip joint causes a dorsal extension of the great toe, much as in Babinski's test. This sign is also present in senile meningitis and edema of the brain. Edelmann (*Wien. klin. Woch.*, Nov. 25, 1920).

If the head is pushed down during examination for Kernig's sign, the response to the latter is exaggerated in cerebrospinal meningitis. Le Dentu (*Paris méd.*, July 30, 1921).

Description of the *chameleon sign* of basilar meningitis, consisting of slow involuntary movements of 1 or both eyes independently of each other. The chameleon is credited with being able to move its eyes separately. Pieraccini (*Riv. crit. di clin. med.*, June 15, 1922).

SEQUELÆ.—After no infectious disease do blindness and deafness remain as permanent injuries oftener than after cerebrospinal meningitis. These conditions can be prevented in many cases by neutralizing the toxin early in the attack.

When the diagnosis is positive no time should be lost, but serum immediately injected.

DIAGNOSIS.—Upon an early diagnosis largely depends the outcome of a given case of cerebrospinal meningitis.

Among 247 cases reported to the New York Board of Health, according to DuBois, the original diagnosis was confirmed in only 48. Tuberculous meningitis was found in 75 and streptococcal, pneumococcal and influenzal meningitis in 9, 2, and 3 cases, respectively. Thirty-seven cases turned out to be infantile paralysis, mainly of encephalitic type. Thirty-six cases, including 19 of pneumonia, were probably called cerebrospinal meningitis on account of neck rigidity and positive Kernig sign.

If symptoms present themselves from which a suspicion of meningitis arises, lumbar puncture should be performed and about 5 to 10 c.c. of fluid withdrawn to establish the diagnosis.

With proper technique, no danger attends tapping of the ventricles or of the subdural space. In many cases the spinal fluid is turbid or opaque, and this has given rise to the teaching that turbid fluid means the presence of cerebrospinal meningitis, while clear fluid means tuberculous meningitis.

This is not always true. Flexner has called attention to cerebrospinal meningitis in which, in the early stages, the spinal fluid is clear, yet is found to contain the *Diplococcus intracellularis*.

A study of 250 cases in Camp Jackson suggested that the disease was primarily a general sepsis, the meninges being secondarily involved. The writers thus learned to recognize it in the premeningitic stage, characterized by general systemic symptoms, lasting from a few hours to a few days, in 40 per cent. of the cases. These symptoms were a temperature rarely above 102°, slow pulse, with vagal irritability. The manner and facial expression of the patients were characteristic; they were dull, apathetic, resented interference; they used the least possible amount of effort to answer questions; the voice was low, and they quickly lapsed back into quietness. The face, and especially the ears, showed cyanosis; the secretions were viscid; the tongue, when protruded, was covered with sticky saliva. The upper respiratory tract was frequently involved; a petechial rash usually appeared very suddenly. In milder cases there was a papular rash like that of chickenpox. There was a lack of balance of the deep reflexes, one side showing an exaggeration while the other showed a normal, diminished, or absent reflex. A lumbar puncture usually revealed a clear fluid with meningococci. W. H. Herrick (Med. Rec., June 29, 1918).

Latent hyperexcitability of the central nervous system is a valuable early sign. It is elicited by having the patient lie down and bend his head down toward his chest 6 or 7 times in rapid succession and flex the trunk on the thighs. With this procedure all the evidences of an established meningitis, with areas of tenderness, are induced at once. The writer found abdominal neuralgia a rather common and misleading symptom of the disease. C. Preioni (Semana méd., Feb. 5, 1925).

The diagnosis of established cerebrospinal meningitis is, as a rule, easily made. The sudden onset of meningeal symptoms, associated with vomiting, suggests scarlet fever, but examination of the throat shows an absence of patches, the so-called "scarlatinal diphtheria" or "scarlatinal necrosis." The tongue is usually coated, but has not the strawberry appearance so common in scarlet fever.

A positive diagnosis of the disease can be made by examining the fluid drawn by lumbar puncture. As a rule, the spinal fluid is turbid or opaque—not clear and transparent, as in tuberculous meningitis. The characteristic *Diplococcus intracellularis meningitidis* described by Weichselbaum is always present. In a few cases the streptococcus and the pneumococcus have been found, but these are the exception. The bacteriological diagnosis, according to Weichselbaum, depends on the fact that the diplococcus is Gram-negative. It is important to remember that the *Micrococcus catarrhalis* is frequently found in the nasal passages; great care must be exercised to differentiate it, both in its relation to Gram staining and also as to its morphological characteristics.

In old people this disease presents a distinct type. The principal differences are the slow beginning of the disease, with prodromal symptoms, a tendency to vomit and headache, early cloudiness of the sensorium, the increased frequency of the pulse inclined to a still greater increase, and, as a rule, a much lower temperature than is usual in epidemic cerebrospinal meningitis. Most marked is the slight degree of stiffness in the neck, while Kernig's symptom is always present early. Herpes is not

present. This disease is not at all common among old people. Reiche (Münch. med. Woch., Sept. 7, 1909).

The characteristic symptoms of acute onset, convulsions, and high fever, and the classical signs of rigidity of the neck and Kernig's sign, do not usually appear in the meningitis of very young infants, excepting very late in the disease. Kernig's sign and rigidity of the neck are absent in from 50 to 60 per cent. of the cases under 2 years of age. Strabismus, usually fleeting, and pupillary inequalities are among the most constant signs of the disease. Hypersensitiveness, especially of the legs, is a cardinal symptom, as also are the pupillary dilatation from pain, on pinching the spine, and a reflex tremor of the whole body or of a group of muscles on setting the child erect or moving its limbs. This tremor, however, usually presents itself during or after the fourth week of the disease. Highly important from the diagnostic viewpoint are alterations in sight or hearing, such as blindness or deafness, following an illness of uncertain nature. In infants a widening of the fontanelles is of great diagnostic value, as showing increased tension of the cerebral fluid. This is often an early sign and a common condition in epidemic meningitis. Ventricular puncture is important in diagnosing all cases showing increased tension of the cerebral fluid, as the cocci are often found here when they are absent in the spinal fluid. Lumbar puncture is essential; but as this means is not always available, and a bacteriological examination requires time, a provisional diagnosis at least should be made from the symptom-complex, so that treatment by serum injection may not be delayed. E. Levy (Med. Klinik, Bd. vi, S. 1569, 1910).

As for the differential diagnosis of cerebrospinal meningitis, the phenomena to be borne in mind as characteristic of the latter are:

vomiting, fever, anorexia, constipation; pupils irregular and do not respond properly; photophobia; opisthotonos, Babinski present, tache present, Kernig present, Oppenheim present; convulsions throughout the disease, and Brudzinski present.

Tuberculous meningitis is the one disease with which epidemic cerebrospinal meningitis is most liable to be confounded. The writer notes the following points of differentiation: In the epidemic form the onset is sudden, while in the tuberculous type it is slow. Temperature, eyes, and pulse are about the same in each disease. The temperature in the tuberculous variety may correspond more nearly to the tuberculous type of fever. Neck symptoms, Kernig's sign, spasm of the extremities, and paralysis are more marked in the epidemic form. Cerebral pressure, as shown by the fontanelles, is more marked in the epidemic type. There is a high leucocyte count in the epidemic type, while there is a low count in the tuberculous variety. We have the history of an epidemic in the one variety, and a history of tuberculosis in the other. In the epidemic variety the cerebrospinal fluid is turbid and contains polymorphonuclear leucocytes in excess, and meningococci. In the tuberculous type the fluid is clear and contains lymphocytes in excess and tubercle bacilli. W. M. McCabe (So. Med. Jour., April, 1909).

In *fermentative gastritis* there are manifest: vomiting, fever, anorexia, constipation; pupils regular and respond to light; opisthotonos absent, no Babinski, no tache, no Kernig, no Oppenheim; the condition may be ushered in with convulsions; Babinski absent.

Another disease with which cerebrospinal meningitis may be confounded is *scarlet fever*. Thus, the following symptoms may be found in

both conditions: Vomiting, fever; mild exanthematous eruption; accelerated heart action, and convulsions during the period of incubation. On studying such symptoms one can note many points in common. Still, the trained eye will at once examine the tongue, which is characteristic in scarlet fever, and which may not even show swollen papillæ in meningitis. In the throat the necrotic, dirty-gray patches, on the tonsils

Technique of Lumbar Puncture.—The child is placed on either side with the spine curved,—this position spreading the vertebræ apart,—in such position that the convexity of the arc formed by the vertebræ is directed toward the operator. Either the space between the third and fourth or that between the fourth and fifth lumbar vertebræ may be chosen for the puncture. An imaginary line drawn through the crest of the ilium



Lumbar puncture made between fourth and fifth lumbar vertebræ.

especially, will be found in scarlet fever, but will be absent in cerebrospinal meningitis. The cervical glands will be swollen and easily palpable in scarlet fever, but not in cerebrospinal meningitis. As a rule, patients with cerebrospinal meningitis cry continuously because of pain. There is usually marked opisthotonos, which is never found in scarlet fever. The pupils show irregularity and sometimes photophobia in cerebrospinal meningitis; in scarlet fever these symptoms are never found. Rhinitis with catarrhal discharge is sometimes an early symptom in this disease.

to the spine affords an easy indication for locating the proper site of puncture.

In making a puncture one should use a needle having a caliber sufficiently large enough to allow the fluid to flow freely. The needle is inserted along the upper border of the spinous process of the lower of the two vertebræ chosen, in a direction almost horizontal and at an inferior angle of 10 degrees to the axis of the spine. It penetrates from 2 to 5 cm., according to the age and development of the child, before the canal is reached,—which can usually be determined by a slight lessening of re-

sistance. The stylet should then be withdrawn. If the fluid does not escape through the needle it should then be withdrawn slightly and the stylet reintroduced to dislodge any obstruction in the lumen. The puncture should be made as simply as possible, laceration of the tissue around the vertebral column and bleeding due to lateral movements of the needle being carefully avoided.

For diagnostic purposes 15 to 20 c.c. should be withdrawn if the fluid is watery and clear. If it is turbid, then the more one withdraws, the better. I have withdrawn as much as 60 c.c.

If the *Diplococcus intracellularis* is found in the spinal fluid, it is important to withdraw as much of the fluid as possible. The site of the puncture should be closed with a strip of adhesive plaster. Strict asepsis must be observed throughout the operation.

The condition of "dry tap" so frequently encountered may be caused by one or more of the following factors:—

1. The caliber of the needle is small and the spinal fluid very thick.

2. Adhesions are present at the base of the brain, preventing the passage of fluid from the ventricles to the subarachnoid space.

3. A successful puncture having been made, a dry tap may follow because of inflammatory adhesions the result of the previous introduction of the needle.

4. Closing of the foramen of Magendie is the most frequent result of the inflammatory process, and results in dry tap.

5. A fibrin clot, or the presence of the cord in front of the needle, may

prevent the outflow of the cerebrospinal fluid.

If a dry tap is noted, one should leave the needle *in situ* and introduce a second needle two spaces lower. If sterile water be injected through the upper needle and then observed to flow out of the lower needle, the needle point is known to be in the spinal canal. The spinal cord in infants terminates at about the level of the lumbar vertebræ. As already stated, introduction of the needle is simplest between the third and fourth or the fourth and fifth lumbar vertebræ. In these interspaces there is no cord; hence no injury can follow. An imaginary line drawn through the crests of the ilia corresponds to the fourth lumbar intervertebral space.

Crohn's apparatus is useful in determining the exact hydrostatic pressure of the spinal fluid. In some cases the pressure is unusually low, while in others it is very high, the latter condition being met when a large quantity of liquid is present.

ETIOLOGY.—During the severe epidemic of the winters of 1905 and 1906 the weather was unusually cold. The precipitation of snow and the amount of frost and ice were far greater than the average in the corresponding zone for many years. With the exception of the two winters associated with this epidemic there had been occasional spells of mild weather in the winter months, which permitted ventilation in the humblest homes. During intense cold such as characterized these two winters, however, people insist upon closing windows and doors tightly, especially when fuel is expensive. The air in some of these houses is stifling, and, especially among the

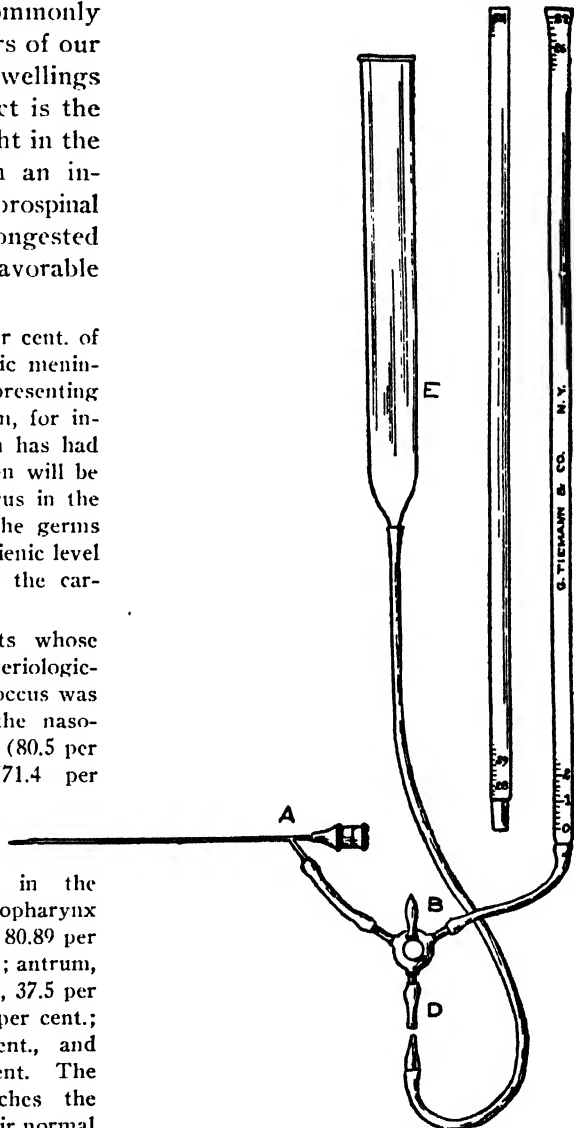
ignorant, it is impossible to persuade those dwelling in them to admit fresh air. Living in such insanitary dwellings is certainly a factor in causing the general depression so commonly seen in the congested quarters of our large cities. A feature of dwellings in the tenement house district is the total absence of direct sunlight in the sleeping apartments. When an infectious disease such as cerebrospinal meningitis enters such congested homes, the germ finds a favorable soil for its dissemination.

According to Debré, fully 25 per cent. of the contacts of a case of epidemic meningitis carry the germs without presenting signs of illness. In a schoolroom, for instance, where one of the children has had meningitis a fourth of the children will be found to harbor the meningococcus in the nasopharynx. The diffusion of the germs is more marked the lower the hygienic level of the environment; in hospitals the carriers are very few.

Among meningitis patients whose upper air-passages were bacteriologically examined, the meningococcus was found most frequently in the nasopharynx (92 per cent.), nose (80.5 per cent.), sphenoidal sinus (71.4 per cent.), pharynx (64.7 per cent.), and ethmoidal cells (61.5 per cent.). Of the structures found involved in the morbid processes the nasopharynx showed 88.31 per cent.; nose, 80.89 per cent.; pharynx, 60.96 per cent.; antrum, 56 per cent.; sphenoidal sinus, 37.5 per cent.; ethmoidal sinus, 30.35 per cent.; frontal sinus, 16.66 per cent., and tympanic cavities, 50 per cent. The meningococcus usually reaches the accessory sinuses through their normal apertures. The frequency of tympanic inflammation increased with prolonged duration of the meningitis. B. Agazzi (Zeit. f. Hals-, Nasen- u. Ohr., Feb. 24, 1923).

In one year the writers saw 7 cases of cerebrospinal meningitis due to the influenza bacillus in children of from

9 months to 4 years. Only one recovered, with residual bilateral deafness. The microorganism seemed identical with that met with in respiratory



Crohn's apparatus for determining the pressure of the cerebrospinal fluid.

tract inflammation. Urech and Schnyder (Ann. de l'Inst. Pasteur, Sept., 1925).

The *Diplococcus intracellularis meningitidis* of Weichselbaum has usually been found the causative agent of

this disease. In some cases a streptococcus, in others a pneumococcus, has been found. Weichselbaum believes that the meningococcus is frequently present, lying dormant in the crypts of the tonsils and pharynx, and, therefore, that when lowered vitality exists, because of subnormal conditions, the meningococcus gains access through the lymph-channels to the meninges and sets up an acute and sudden infection. In addition to the presence of the meningococcus in the tonsils, this pathogenic microbe is frequently found in the nose, whence it probably gains access through the frontal sinuses to the brain.

The meningococcus reaches the ventriculo-subarachnoid system through the choroid plexus. In fulminating cases Dopter found an acute inflammation of the plexuses. The ventricles are considered the essential site of infection, and treatment should be by intraventricular injection as well as through spinal puncture. Lewkowicz (Lancet, Sept. 6, 1924).

The meningococcus can be transmitted and an infection disseminated by direct contact with secretions containing it. Weichselbaum does not believe that the sudden appearance of a case of cerebrospinal meningitis in an otherwise healthy locality is extraordinary when the etiological conditions, *e.g.*, the possibility of harboring this diplococcus in the nose and throat, are remembered.

A connection between body lice and meningitis noted in 2 epidemics. Measures to eradicate lice are indicated, with isolation until meningococci no longer occur in the blood. Pizzini (Policlinico, May, 1917).

PROGNOSIS.—Not very many years ago 80 per cent. of the patients died and about 20 per cent. recovered. Of those that recovered, many were

blind or deaf. Since the introduction of the Flexner serum, the recoveries range between 70 and 80 per cent., and the mortality between 20 and 30 per cent. One must not look for equally good results unless treatment with the serum is commenced very early. In a case of mine an infant 1 year old had been ill nine days before the serum was injected. The disease continued for seven weeks, the infant then recovering.

According to Cohn, a perfect clinical recovery takes place in all mild cases. A complete recovery without subsequent troubles is possible even in the severer and worst cases. The probability of a recovery which will leave no trace is greater in children than in adults. In the latter, sequelæ may appear 2½ years after the disease. After an apparent convalescence has lasted 4 weeks the onset of hydrocephalus is possible. The complication most to be feared is deafness. While all paralytic symptoms may be recovered from and a choked disc may disappear, deafness is irreparable.

Case in which there were 2 relapses, the first occurring 20 days after the initial meningal reaction (which lasted 8 days) and the second after an interval of 2½ months. In the first 2 attacks no meningococci could be found in the spinal fluid or blood, although herpes and purpura testified to a general infection. During the second relapse, which lasted a month, meningococci were found. In this attack a marked difference in the amount of sugar in the spinal fluid at the beginning and end of a lumbar evacuation was observed. This "anisoglycorrhachia" the writer deems significant in the development of the disease. C. Zøller (Bull. Soc. méd. des hôp. de Paris, Nov. 20, 1925).

TREATMENT.—Lumbar puncture should be performed. This will relieve the excessive intracranial pressure, besides draining the ventricle of pathogenic material. Immediately after such lumbar puncture the Flex-

ner antimeningitis serum should be injected. If one is dealing with a young infant in which lumbar puncture has resulted in a dry tap, **aspiration of the lateral ventricles** through the open fontanelle should be performed, and the serum injected through the needle left *in situ*.

For general use a **polyvalent anti-meningococcus serum** is probably best. The amount required depends upon the course of the disease; a total of 600 to 800 c.c. has been given without ill effects. Relapses are not very frequent after serotherapy. Drugs or other methods, if used, must be combined with it. Rinsing out the spinal canal with normal salt solution has not proven satisfactory. Nearly all workers advise an **autogenous vaccine**. When this cannot be obtained, a **polyvalent vaccine** containing representative strains of meningococci may be substituted. The dosage varies considerably. Vaccines are chiefly recommended in the subacute or chronic stages, when serum seems to have become inefficient. K. D. Blackfan (Medicine, May, 1922).

In subarachnoid block, **cistern puncture** was employed successfully by the writers in an infant aged 4 months. Repeated injections of 5 to 8 c.c. of serum were thus made. A. G. Mitchell and J. J. Reilly (Amer. Jour. Med. Sci., July, 1922).

Where specific antimeningococcus serum is unavailable, **normal horse serum** intravenously and intraspinally will give useful results. The doses needed vary considerably. Relapse readily occurs, apparently owing to lack of development of specific properties in the blood. Monteiro (Rev. med.-cir. do Brasil, Nov., 1922).

Report of a septicemic case in which **protein therapy** by means of a single injection of **milk** resulted in complete recovery. Blum (Bull. Soc. méd. des hôp. de Paris, Jan. 25, 1923).

The author has had the most rapid recoveries where he has been able to introduce 50 c.c. of **serum** intrathecally

and 25 c.c. intravenously on at least 2 consecutive days. Between 30 and 60 c.c. of spinal fluid can generally be safely withdrawn. It is well always to introduce a little less serum than the amount of fluid withdrawn; warmed to 100° F., it is allowed to gravitate into the spinal canal from a height of about 6 inches. The pulse is carefully watched and introduction stopped instantly if there are signs of collapse. After injection it is important to elevate the foot of the bed 18 inches for about 2 hours. In infants the writer usually adopts the expectant method (1 initial dose followed by watching, with repetition as symptoms may require), and gives a little **bromide** throughout the treatment. Infants do not bear injections well, being liable to suffer convulsions. Girdwood (Med. Jour. of So. Africa, Aug., 1923).

The writer had a mortality of 16 per cent. in his 50 cases in children in the last 15 years. His results have been better since he has given 5 or 6 daily intraspinal injections of the **serum**, and then suspended it. If the fever keeps up, he resumes the injections, watching for symptoms of anaphylaxis. If the meningitis persists, repeated **hot baths** and an **autogenous vaccine** may prove useful. Such treatment seems to ward off the sequelæ of the disease. L. Morquio (Arch. Latino-Amer. de Ped., xviii, 420, 1924).

Case in an infant in which complete recovery was obtained although **serum** was not begun until the neck had been rigid 20 days. In the first 6 days a total of 60 c.c. was injected intramuscularly and 120 c.c. into the ventricles, with 20 c.c. more in the 3 succeeding days. J. de Cardenas y Pastor (Arch. españ. de ped., Jan., 1926).

In lumbar puncture the object is to aspirate as much of the spinal fluid as possible. Through the same needle I then inject from 30 to 60 c.c. of Flexner's serum. The serum should be warmed before injection, and should be introduced slowly. It

is well to elevate the hips and lower the head when injecting the serum. Daily injections of 30 to 60 c.c. are required if no improvement is noted.

In meningococcus septicemia, which may be unattended with meningeal symptoms, repeated intravenous serum injections have been used with apparent benefit.—Ed.

Untoward results in the **serum** therapy of cerebrospinal meningitis are as uncommon as in other infectious diseases. The anaphylactic symptoms that sometimes appear, such as headache, cardiac weakness, albuminuria, exanthemata, disturbances of the bladder and rectum, fever, pains in the joints, and edema, soon pass away without leaving the least permanent injury. Better results are to be obtained by the administration of a single large dose than by the use of many small doses. Schepelmann (*Wiener klin. Woch.*, Jan. 26, 1911).

Success depends on commencing treatment early, injecting the **serum** into the spinal canal, with not too small doses. The treatment is aided by **raising the foot of the bed** for 15 to 20 cm. for twelve hours after each injection. It seemed to be borne without discomfort by the patients, as a rule, but **morphine** had to be given in a few cases. The patients usually regained consciousness after the injection, the cerebrospinal fluid cleared up, and the condition grew progressively better. In 2 cases initial optic neuritis retrogressed under the serotherapy. Jochmann (*Deut. med. Woch.*, Sept. 21, 1911).

The writer had 20 cases of cerebrospinal meningitis in his charge at Athens during the recent epidemic. Under **serotherapy** all the children recovered with one exception, the mortality thus being only 7.14 per cent. A. Papapanagiotu (*Archives de méd. des enfants*, Nov., 1911).

After five years' trial the **Flexner serum** has proved its germicidal properties in the meningococcic form of the disease. It has shown this by re-

ducing a mortality that was formerly between 75 and 80 per cent. to one that is now between 25 and 30 per cent., and by the less frequent presence of complications and after-effects. Hynes (*Amer. Jour. of Obstet.*, May, 1912).

In older children the diagnosis is not so difficult as in the younger, and the prompt use of the **Flexner serum** treatment has greatly improved the prognosis in such cases. In young infants the symptoms are masked and the dread of making the lumbar puncture needlessly has deterred many from using this valuable method. Particularly difficult are the cases complicated with pneumonia, which itself is attended with cerebral symptoms. Many intestinal disorders show misleading symptoms in infants. While a day's delay is not dangerous with older children, it may be fatal for the baby. H. Koplik (*Jour. Amer. Med. Assoc.*, June 7, 1913).

The writer has used serum in 226 cases since 1907. The mortality was only 12.5 per cent. Before the use of serum, the mortality was 48.5 per cent. in sporadic cases and 83.3 per cent. in the epidemic form. The value of serum is further shown in the attenuation of the symptoms, the rarity of complications, and the rapid recovery. Netter (*Bull. de l'Acad. de Méd.*, June 29, 1915).

From the results obtained by the **intramuscular injection** of serum in 12 cases of cerebrospinal meningitis the writer concludes that this method is equally as efficacious as the intraspinal. It suffices to give 10 c.c. (0.66 Gm.) every 24 hours, or in grave cases every 12 hours until 30 or 40 c.c. (2 to 2.66 Gm.) have been administered. Its action is more satisfactory when given early in the disease, and when a case is seen late in its course it is preferable to do a lumbar puncture followed by an intraspinal injection to obtain a more rapid effect. Fanciulli Francesco (*Gaz. degli ospedali e delle cliniche*, Oct. 4, 1917).

The results of serum treatment in the Royal Navy showed that of the several types of serum used that prepared by Flexner was the only one very effective. In cases not treated by serum the mortality was nearly 53 per cent. as compared with 27.5 per cent. for those treated with **Flexner's serum**.

The earlier in the course of the disease the serum was begun, the better were the results.

The administration of the serum was associated with serum rashes in about 60 per cent. of the cases surviving for over 10 days. Rolleston (*Lancet*, Jan. 19, 1918).

In a series of 417 cases of epidemic cerebrospinal meningitis treated in Hong-Kong, 104 patients did not receive either serum or lumbar punctures, obtaining merely the usual Chinese treatment. Of this number 84.6 per cent. succumbed. Among 228 patients receiving Chinese treatment but also one or more lumbar punctures, the mortality was 51.1 per cent. Among 14 patients treated by lumbar puncture only the mortality was 57.1 per cent. Among 71 patients receiving 1 to 5 lumbar punctures and also a more or less incomplete serum treatment the mortality was 45 per cent. Olitzky (*Journal of Tropical Medicine and Hygiene*, Feb. 15, 1919).

Flexner's serum must be administered reasonably promptly. One must ascertain the type of coccus at the earliest possible moment, give enough serum, and resolutely adhere to the treatment. Hine (*Brit. Med. Jour.*, Sept. 18, 1920).

Before performing *intracranial* injections the scalp should be shaven and prepared with the usual aseptic precautions. The aspirating needle must be rendered sterile by boiling. It is then pushed through the anterior fontanelle downward and inward into the ventricles of the brain, at least 1 inch or more. The needle is inserted about $\frac{1}{4}$ inch to one side of the longitudinal

sinus. Kocher advocates puncturing through the frontal lobe at a point $2\frac{1}{2}$ cm. from the middle line and 3 cm. anterior to the central fissure—a point lying somewhat in front of the bregma. The needle must penetrate 4 or 5 cm. before it reaches the ventricle, and should be directed somewhat downward and backward. The ventricle in this situation is broad, extending fully 2 cm. from the middle line, and there is practically no risk of hemorrhage during the passage of the needle. With experience, and after practice on the cadaver, punctures may be safely made not only at the point of Keen and Kocher, but elsewhere if need be—through the anterior pole of the frontal lobe, through the pole of the occipital lobe, etc.; these methods, however, are more hazardous than those detailed above, and should be undertaken only by operators particularly familiar with intracranial work.

In infected cases with a beginning external meningitis there is always a certain risk of inoculating an uninfected ventricle. The same accident has occurred owing to the passage of an occluded needle through an abscess and then into the ventricle. A trocar should not be used. It is advisable to employ a needle with a rather blunt point, which will pass by vessels without cutting them. The opening in the needle should be on the side and not upon the point, lest it become plugged with brain matter.

Report of the recovery of 3 out of 4 infants, 5 to 7 months old, with severe epidemic meningitis under **serum** treatment.

The serum was injected directly into the spinal cavity to the amount of 150 to 160 c.c. in about 8 daily injections.

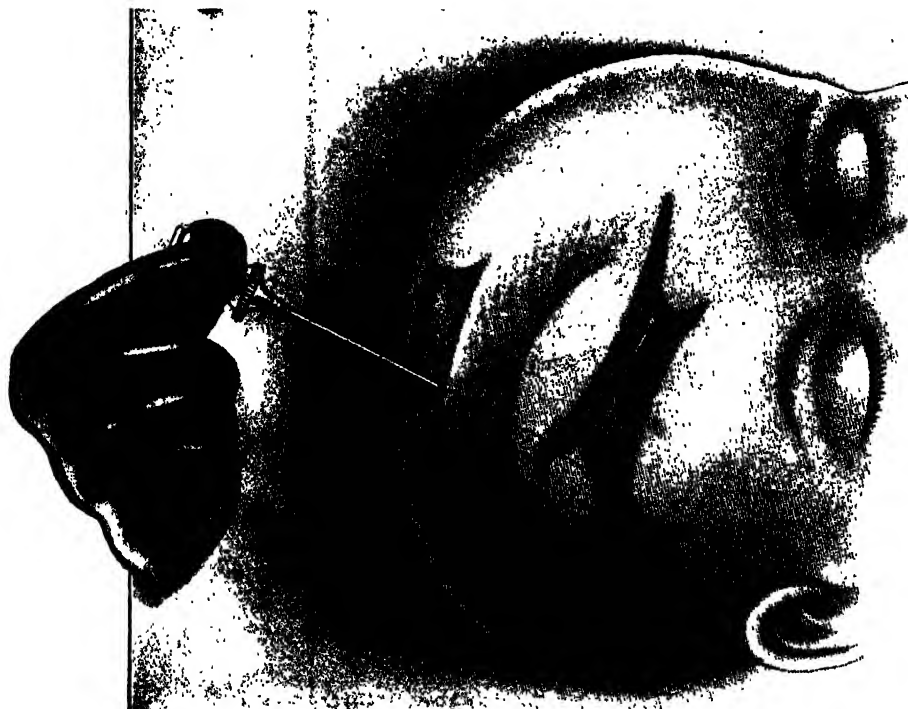
Up to 200 c.c. can be given to young infants without harm. Intolerance

does not develop usually until after several injections, with improvement far advanced.

The meningococci disappeared after 2 or 3 injections.

Where intraspinal injection is not practicable, or pyocephalus develops, the serum can be injected directly into the lateral ventricle.

was resorted to, a pint of normal saline solution being used. After as much had been drained off as possible, 50 c.c. of Flexner's serum were injected. This plan of treatment was successfully carried out in 2 of my cases. In both, lumbar puncture had yielded a dry tap.



Translucent head of child. The needle is entering the outer angle of the anterior fontanelle and penetrating the lateral ventricle, which is seen in shaded outline. The falx is dimly seen. The light line running from before backwards is the septum lucidum separating the two ventricles. (Fischer.)

An **autogenous vaccine** by the vein may usefully supplement serotherapy in the graver cases. F. de Angelis (Pediatria, Mar. 15, 1921).

In the Babies' Wards of the Sydenham Hospital, New York, there have been aspirated many times 50 c.c. of purulent fluid containing the *Diplococcus intracellularis* in almost pure culture. Using the same needle, or one having a larger caliber, irrigation

The purulent discharge gradually lessened and the meningococci gradually disappeared after serum injections continued over a period of four weeks.

A decided reaction followed each injection of serum, the child changing in color during the injection from a waxy pallor to a uniform and universal red flush. One-half hour after the injection, the child remained flushed, perspired profusely, and had

some frothy mucus at the mouth. The pulse rate was increased, the volume improved, and the tension was much higher. The leucocytes were invariably increased; the polynuclear leucocytes were the ones especially augmented, while, as a rule, the mononuclear leucocytes and the lymphocytes were reduced within six hours after the serum injection.

In the treatment of fever in cerebrospinal meningitis antipyretic measures, such as **cold packs**, an **ice-bag** on the head, and **tub baths**, are indicated. The coal-tar products, because of their depressing effect upon the heart, should be avoided. **Cupping** of the **neck** and **spine** sometimes relieves internal congestion.

Eliminative treatment is also indicated, and consists in cleansing of the gastrointestinal tract with the aid of **citrate of magnesia** or **calomel**. When high fever exists, flushing the rectum and colon with a **cold soap-suds enema** will be found useful.

As for medicinal treatment, to relieve the vomiting **cracked ice** should be given, in addition to 1-grain (0.06 Gm.) doses of **menthol**. To relieve muscular spasm, twitching, and delirium, **hyoscine hydrobromide** in doses of $\frac{1}{6000}$ to $\frac{1}{300}$ grain (0.00001 to 0.0002 Gm.) should be given, and repeated every few hours. **Morphine** hypodermically, in doses in $\frac{1}{50}$ grain (0.0012 Gm.), gradually increased, is also valuable. **Leeches** applied at the nape of the neck, over the mastoid portion of the temporal bone, or at the *alæ nasi*, will sometimes relieve. **Sodium bromide** in 5- to 30- grain (0.3 to 2 Gm.) doses may be given until the systemic effect is noted. **Codeine**, $\frac{1}{10}$ grain (0.006 Gm.) gradually increased until $\frac{1}{2}$ grain (0.03

Gm.) is given, will frequently soothe the nervous system. The sedative effect of a **warm bath** is also generally recognized. The bath should be given at a temperature of 100° to 105° F. in a bathtubful of water to which $\frac{1}{4}$ to $\frac{1}{2}$ pound (200 to 400 Gm.) of sulphur has been added. Such a warm **sulphur bath** may be given twice a day. The duration of each bath should be at least ten to thirty minutes.

Unless the strength is supported by food the patient will die of exhaustion. **Feeding** by mouth with **peptonized milk**, **broth**, **gruel**, and **eggs** is indicated. If, however, there is vomiting and the stomach does not retain food, **rectal feeding** should be resorted to at intervals of three or four hours.

After-treatment.—If the case progresses favorably, careful attention must be given to restorative treatment. **Codliver oil**, **Fowler's solution**, **sodium iodide**, and the **hypophosphites** must not be forgotten. **Electricity**, combined with **massage** and **sea-salt bathing**, is also indicated during convalescence. **Milk**, **cream**, **butter**, **eggs**, and **cereals** should form the bulk of the restorative nutriment administered. A decided **change of air**—from the city to the seashore or to the mountains—will prove beneficial.

Prophylaxis.—**Isolation** of the case is an important feature in this connection, and also, where at all possible, healthy germ carriers.

During the first three months of 1909, 139 cases of epidemic cerebrospinal meningitis developed in 45 garrisons throughout France, with 38 deaths. The patient was isolated and his two neighbors in the dormitory were also isolated for fifteen days, and

all the men in the dormitory were kept apart from the other troops and were examined for the germs. The rooms were disinfected. Among 372 men thus isolated, 72 germ carriers were discovered, but only 1 of these carriers developed the disease later. L. Vaillard (Bull. de l'Acad. de Méd., Apr. 27, 1909).

A high carrier rate usually denotes overcrowding and dangerously unhygienic conditions, even though no cases of the disease may have recently occurred. Whilst sporadic cases may occur in a military as in any other community with any carrier rate, anything approaching an epidemic of cerebrospinal fever is heralded by a warning rise of considerable height in the carrier rate. Severe overcrowding will probably be accompanied by a carrier rate (serological) of at least 20 per cent. A carrier rate of this height will usually imply that the mobilization standard of 40 square feet per man has been infringed, and that beds in the unit examined are less than 1 foot apart. It should be regarded as a signal for prompt and effective action to diminish overcrowding and to improve ventilation. The distance between beds is of paramount importance. Carrier rates from 2 to 5 per cent. may be considered usual under the best conditions obtainable in barracks and hutments. When a unit shows a high carrier rate, a distance of at least $2\frac{1}{2}$ feet between the beds should be enforced. Recruits should be specially spaced out during their first three months of service. Capt. J. A. Glover (Brit. Med. Jour., Nov. 9, 1918).

LOUIS FISCHER,
New York.

MENSTRUATION, DISORDERS OF.—Menstruation may be *defined* as a periodic discharge of sanguineous fluid from the genital tract of a woman, occurring during the period of sexual activity, from puberty to the menopause.

This definition makes no attempt to deal with the etiology of this function, which has been the subject of much speculation and many theories for many years. Probably the oldest theory of menstruation is the toxic, or chemic, which holds that certain materials which would otherwise be injurious to the organism are eliminated by this discharge. Another old theory was that the flow results from plethora. As the woman had to nourish the unborn babe, she was supposed to be endowed with superior blood-making power, and, if pregnancy did not occur, the periodic vent for superfluous blood appeared.

These various theories may be reviewed in a brief manner. The theory supported by Pflieger, Bischoff, and others holds that menstruation is dependent upon ovulation and coincident with it. On the other hand, Ruge maintained that ovulation and menstruation are two entirely independent functions.

Later, Fränkel promulgated the view that the act of menstruation is governed by the corpus luteum. According to Montgomery, the investigations of Fränkel justify the following theory regarding the corpus luteum and its influence on the menstrual function:—

1. The corpus luteum is a gland with an internal secretion. Following each ovulation, this gland is re-developed in the functioning ovary and its secretion dominates the occurrence of menstruation.

2. The secretion of the corpus luteum entering the blood determines the nutrition of the uterus, especially of the endometrium, in whose connective tissue it excites extreme hyperplasia and hyperemia.

3. It prepares the uterus for the reception, retention, and nutrition of the fecundated ovum and, where fecundation has not taken place, establishes the menstrual flow.

Fränkel showed that removal or destruction of the corpus luteum prevents the next menstrual flow, and that abortion occurs when the corpus luteum is destroyed early in pregnancy. Late in pregnancy, on the other hand, growth of the ovum is not disturbed by removal of the corpus luteum.

The mechanism of menstruation is better understood than its causation. Veit, as a result of a study of the uterus during this period, divides this phenomenon into three periods:—

1. Premenstrual congestion, in which the capillaries are distended; there is a transudation or exudation of blood into the intercellular tissues, the meshes of which are widened, and an accumulation of blood under the subepithelium, which is raised into little hillocks by the subepithelial hematomata.

2. Escape of the accumulated blood through the interstices between the epithelial cells, which are pushed apart; some of them may be carried away by the blood as it forces its way out. There is also some desquamation of glandular epithelium.

3. Postmenstrual involution, in which the mucosa shrinks and the extravasated blood remaining in the intercellular tissue is absorbed. The surface epithelium, raised from its subjacent tissue, sinks again to its normal level.

There are 4 phases of the blood-picture: The normal or intermenstrual, lasting an average of 13 days; the premenstrual, about 6 or 7 days, and the

menstrual and postmenstrual, each lasting about 4 days. There is an average increase in the red cells of 180,000 before the start of menstruation. During menstruation the red cells are slightly decreased from normal. At the beginning of the postmenstrual period the number increases again, then gradually falls until it reaches the intermenstrual period. The leukocytes are lowest during menstruation, with a decrease in the polymorphonuclears. The basal metabolism progressively increases until just before menstruation, when it is diminished. Ludlum and McDonald (Surg., Gyn. and Obst., Nov., 1925).

The menstrual blood is dark in color, alkaline in reaction, and, owing to the presence of mucus, does not coagulate unless it is excessive in amount. The discharge of mucus before and after the flow of blood is an essential part of the menstrual flux; in fact, in the lower animals the menstrual flow, if present at all, is entirely of mucus. The average duration of the flow is four to five days, but the length of the period varies in different women. When once an individual standard has been established, any marked deviation from it usually indicates some local or constitutional disorder.

It is difficult to estimate the amount of blood lost at each period. Authorities vary in estimating it from 2 to 8 ounces. Menstruation in the majority of women occurs every twenty-eight days, and the intervals may vary from twenty-one days to five or six weeks.

The onset of menstruation, or the time of its first occurrence, is influenced by race, climate, mode of life, heredity, and genital sense. In a series of 1000 cases studied by Krusen the average age of puberty was 14½ years. It is seen earliest and

latest in cold climates. The peculiarities of this function vary in different families. In women of strong sexual proclivities menstruation is commonly established earlier and lasts to a greater age.

The general phenomena of menstruation are as follows: Slight elevation of pulse rate and temperature at the onset; also a tendency to slight physical depression and lassitude. The breasts and thyroid gland are often swollen and enlarged. Belfast asserts there is an increase of weight for a few days before the flow, an increment which is due to increased absorption of oxygen and to decreased elimination. There is a sense of weight, pressure, or uneasiness in the lower extremities and pelvis. General nervous excitation may be noted, and often gastrointestinal disturbance will occur. Kelly states that to define what constitutes a normal status during menstruation is difficult and that it would seem that a certain amount of pain and discomfort must be accepted as the routine condition of things for the majority of women, and the question to be answered is, therefore, At exactly what point does suffering become pathological?

VICARIOUS MENSTRUATION.

The term vicarious menstruation is inaccurate, if menstruation implies the casting off of endometrial elements, and can only be justified as a convenient one to describe the hemorrhage which appears from some other part of the body than the uterus in response to the menstrual molimen. The term is used to describe that want of co-ordination in the internal secretions, or their action, whereby the uterus does not

menstruate, but there is a flow of blood from some other part of the feminine anatomy which replaces that which should come from the genital tract.

The history of these cases is often vague and unsatisfactory. Many unusual phenomena are observed at the time of the menstrual period which may be described under this caption. Changes may occur in the mammary glands with hemorrhage from the nipple, or periodic discharge of colostrum on pressure. Local and functional changes in the eyes may be noted. The organs of nutrition may be affected and intestinal hemorrhage replace the menstrual flow. Disturbance of the skin, with acne of the face, pigmentation of the skin, herpetic eruptions, purpura, etc., may be characteristic in some individuals. These cases must not be confounded with those in which a patient may lose blood from some diseased organ, such as the lung or stomach, and the mistake be made of considering that the bleeding is the consequence of the amenorrhea instead of its cause. Sometimes the weak point is found in a nevus. Lermoyez has reported the case of a girl who had a periodic discharge of non-coagulable blood from the right ear. After the normal menstruation was established, the aural discharge rarely occurred. According to C. A. L. Reed, vicarious hemorrhage is most common from the nose; next in order of susceptibility come the stomach and intestines. Hancock has reported a case of bleeding from the left breast preceding each period.

TREATMENT.—The treatment of vicarious menstruation is to establish a flow from the uterus by the

measures recommended for amenorrhea. Seeligman advises the use of a **hot douche** during the term supposed to correspond to the intermenstrual periods. Where normal menstruation cannot occur, the unusual bleeding is a safety-valve which it is not wise to shut down. Occasionally the bleeding is so profuse from the abnormal site that radical measures are indicated, such as removal of the ovaries.

PRECOCIOUS MENSTRUATION.

This term is applied to premature menstruation. A flow of one to five days' duration must recur at regular intervals and be associated with the various feelings of discomfort analogous to those experienced by women at the catamenia, in order to be classed as precocious menstruation. Precocious maturity involving a rapid growth of the whole body in weight and height, with changes in the genital organs and mammary glands, and with the growth of hair above the genitals and in the axilla, usually precedes the menstruation. Precocious menstruation is not uncommonly associated with nymphomania. Heredity plays a prominent rôle in its occurrence, and ovarian tumors, not infrequently of a sarcomatous type, have been observed.

Strassman has collected 15 cases of menstruation beginning in the first year of life. **Bad habits** and immoral associations tend to premature development of the genital sense and **should be corrected**. **Masturbation should be prevented** by careful supervision of the child and by the relief of local irritations. **General rest and time treatment and removal from nervous excitement** are advised.

For AMENORRHEA, see Volume I.

For DYSMENORRHEA, see Volume IV.

MENORRHAGIA AND METRORRHAGIA.

Menorrhagia is the term applied to abnormally profuse or abnormally prolonged menstruation. *Metrorrhagia* is irregular uterine hemorrhage at odd times without distinct periodicity. As these cannot be applied always with accuracy, it is well to employ the simple term of uterine hemorrhage to designate the abnormal flow of blood from that organ; and as precisely the same causes give rise to both classes of symptoms, they may be conveniently discussed together. Before deciding what constitutes an excessive loss of blood, it is necessary to adopt at least an approximate standard of the normal amount for the individual. Each woman is familiar with her individual norm and can easily determine deviations from it.

ETIOLOGY.—In menorrhagia the flow may be excessive throughout the usual period, or the flow may be unduly prolonged beyond the normal limits. The causes of uterine hemorrhage may belong under two classes: 1. Local or pelvic. 2. General or constitutional. It is important to emphasize the fact that all cases of abnormal or irregular bleeding from the genital tract should be the subject of careful examination to determine the cause. To neglect this investigation means increased morbidity and mortality from pelvic disease. The local causes may be uterine or extrauterine. Among those affecting the uterus itself are abortion, threatened or incomplete; mucous or fibroid polypi; submucous fibroids; carcinoma of the cervix or corpus uteri; sarcoma; chorioepi-

thelioma; acute and chronic endometritis; subinvolution of the uterus, and retrodisplacements of the uterus. Tuberculosis of the endometrium is one of the rarer causes of menorrhagia. Sclerosis or atheroma, and calcification of the uterine blood-vessels are noted in women nearing middle life or after the menopause, and are factors in unusual bleeding.

In 62 cases of uterine hemorrhage under the age of 19, Theilhaber found the uterus unusually small in 58; in only 4 was it of normal size. Excessive hyperemia in an insufficient musculature is liable to entail hemorrhage from it, and sexual excitement, maintaining the hyperemia in the uterus, is an important factor in uterine hemorrhage. Masturbation is prevalent among women, and the uterus accommodates itself poorly to frequent sexual excitement.

The causes of excessive or untimely bleeding from the uterus are grouped by the writer into those: (1) Of endocrinal origin—as the puberty hemorrhages. (2) Due to changes in the uterine tissues (static factors) enlarging the area in the uterus which responds to the ovarian impulse, *e.g.*, descensus, retroversion, etc. (3) Due to new growths in the uterine wall. (4) Due to disease in adjacent organs which increases the premenstrual congestion. (5) Not preceded by amenorrhea or following the menopause—usually of polypoid or malignant origin. (6) Occurring in the course of pregnancy.

In cases of deficient thyroid function there is often an increase in the menstrual bleeding. Excess of ovarian impulse is most commonly found at puberty or near the menopause, in such local conditions as prolapse of the ovary, retention cysts or cystic degeneration. Clots always signify some abnormality, and true menorrhagia is always attended by considerable clotting. J. O. Polak (*Atlantic Med. Jour.*, Feb., 1925).

The extrauterine causes are extrauterine or ectopic pregnancy, in which menorrhagia is a striking symptom and

early diagnosis is imperative; diseases and neoplasms affecting the ovaries (hyperplastic ovaries, follicular cystic disease) and oviducts, and pelvic hematocele.

Dalché has called particular attention to syphilis as a cause of hemorrhage after the menopause, particularly that diffuse syphiloma which may form large uterine or periuterine masses simulating cancer or fibroma.

Hemorrhage from the genital organs is not always due to uterine disease. Occasionally there is noted an excessive menstrual flow just after the establishment of puberty. There is also a menorrhagic chlorosis accompanied by hemorrhage. Other conditions which produce it are lithemia, mitral stenosis, hypothyroidism, partial myxedema, and even dyspepsia. Any liver disease may be accompanied by genital hemorrhage. Arteriosclerosis in women at the climacteric may cause hemorrhage of an alarming nature, leading to the fear of malignant disease. Pouliot (*Jour. de méd. de Paris*, July 6, 1912).

A form of functional menorrhagia due to hyperthyroidism is recognized by the author. The chief symptoms in his cases were loss of weight and nervous instability, and less constantly, increased pulse rate, slight tremors, and a tendency to sweat easily. Thyroid enlargement was occasionally present, and exophthalmos in but 1 case. He divides the cases into 2 groups: (1) Six cases at or near puberty, with normal or depressed basal metabolic rate in 5 out of 6, in spite of considerable thyroid enlargement in some of them. (2) Fourteen sexually mature cases, all with raised basal metabolic rate (+14 to +46 per cent.). In the second group, X-ray treatment of the thyroid gland reduced the metabolic rate to within normal limits (—10 to +10), and menstruation returned to normal in 8 out of 10 cases treated. In the other 2, the

metabolic rate remained high and there was no menstrual improvement. Out of 4 of the 6 cases at puberty treated, 3 were unimproved. A. W. Bourne (*Med. Press and Circ.*, Jan. 18, 1922).

The general or constitutional diseases causing uterine hemorrhage are anemia in exceptional cases, hemophilia, scurvy, gout, phthisis in the early stages, the acute infectious fevers, malaria, influenza, saturnism, cardiac diseases causing vascular stasis, and hepatic diseases with portal stasis. In fact, any general disorder that will impede the return flow of blood from the pelvic viscera will cause an unusual vascular pressure that may result in hemorrhage from the uterus. In obscure cases the possibility of syphilis must be borne in mind and the Wassermann reaction utilized.

The practitioner should not rest satisfied until he has determined the cause of hemorrhage in his patient. If the diagnosis is not clear, it is best to employ an anesthetic and make a thorough examination of the uterus and other pelvic structures and, if necessary, dilate and curet and explore the interior of the uterus and examine suspected tissue microscopically in order to make a scientific and accurate diagnosis. It is only by such thorough investigation that carcinoma, one of the most important causes of irregular bleeding, can be detected early and the mortality from this scourge of womankind be reduced.

TREATMENT.—The first step toward effectual treatment is correct diagnosis and recognition of the cause of hemorrhage. The treatment may be general or local. By general medicinal treatment we mean the administration of such drugs as **pituitary extract**, **ergot** and its derivatives,

hydrastinine, **cotarnine hydrochloride (stypticin)**, **viburnum prunifolium**, and **adrenalin**. When some systemic disturbance, *i.e.*, cardiac or hepatic disease, is the causative factor in the bleeding, appropriate constitutional measures must be instituted. All drugs administered by mouth should be considered as of only temporary value and as being used only to tide the patient through a period until the proper local measures are adopted for the permanent relief of the patient.

Where rapid action is required, **pituitary solution** may be injected hypodermically in doses of 16 minims (1 c.c.), repeated every 3 or 4 hours.

In active bleeding the patient should be at **rest in bed**, and **bromides** or other sedative given where restlessness exists.

Pituitary extract (posterior lobe) recommended in metrorrhagia of emotional origin or at the menopause. The writers use a liquid extract in an initial dose of 0.5 c.c. (8 minims), followed by 5 to 7 more doses of 1 c.c. (16 minims) each into the gluteal muscles on alternate days. Capsules may be prescribed instead. The measure was also found useful in menorrhagia at puberty, the extract being injected a few days before the expected period. The action is ascribed to vasoconstriction in the uterus and ovaries, contraction of the uterus, and checking of the ovarian internal secretion. The heart, blood-pressure and urine should be examined before prescribing the drug, as it raises the blood-pressure. Mossé and Fabre (*Gynéc. et obst.*, Mar., 1922).

According to Mouralov, a few days of mercurial medication, even in the absence of syphilis, will sometimes act strikingly in overcoming metrorrhagia. Nufiez, in unaccountable metrorrhagia of 10 or 15 days' duration in nulliparæ, observed benefit from injection of 10 or 20 c.c. of **antistreptococcus**

serum each month for 2 or 3 months. Similarly, Busse witnessed early cessation or marked reduction of bleeding in obstinate cases upon subcutaneous injection of 10 c.c. of **human serum**.

In 29 cases Kroemer had success with **gelatin injections** in conjunction with ingestion of **sodium chloride** in doses of 4 to 5 Gm. (1 to 1¼ drams) 3 times a day; the treatment also showed prophylactic value. F. Hare found in several cases that a single administration of 3 minims (0.2 c.c.) of **amyl nitrite** at 3 or 4 successive menstrual periods was followed by permanent relief; where it failed, a course of **nitroglycerin** given during the period was usually sufficient. According to Whitehouse, **purgation, nitroglycerin** and **diet** are of value where the bleeding is due to high blood-pressure, and purgation likewise in hepatic cirrhosis. Where the calcium index is low, **calcium lactate** is of service.

Excessive menstrual discharge in young girls, due to blood changes, is often arrested, according to Huchard and Fiessinger, by the following:—

R. Subcarbonate of

<i>iron</i>	gr. iss (0.1 Gm.).
<i>Ergotin (Bonjean)</i> ..	gr. ¾ (0.05 Gm.).
<i>Quinine hydrobromide</i>	gr. ⅙ (0.01 Gm.).
<i>Extract of belladonna</i>	gr. ½ (0.005 Gm.).

M. Ft. in pil. no. j.

Sig.: Two pills before meals.

Subcutaneous injections of pituitary extract proving ineffective in obstinate cases, the writer resorted to **injections of pituitary extract** directly into the uterine muscle itself. After antiseptic preparation of the parts, the anterior lip of the cervix was fixed with a double tenaculum—not drawn forward, however, or but slightly—and a hypodermic needle introduced into it to a depth of 1 or 2 cm. in a direction parallel with the long axis of the uterus. The barrel of the syringe was removed for a moment, to make sure that no blood-vessel had been entered by the needle, then reapplied, and the injection made. C. Koch (*Semaine méd.*, Jan. 8, 1913).

In metrorrhagia in virgins **repeated dipping of the hands in very hot, almost boiling, water** generally proves effective as a remedial measure. **Rest in bed**, with or without **heliotherapy** or exposure to **sunlight**, is indispensable. An **ice-bag** should be kept on the lower abdomen. **Calcium chloride** and **opium** may with advantage be used internally. **Vaginal injections** should be given first at room temperature then cold; they are not indispensable except to wash out clots that are beginning to undergo putrefactive changes. **Thyroid preparations** in moderate doses give good results; **mammary** or **adrenal organotherapy** also sometimes proves serviceable. **Blistering over the liver** brings about arrest of some refractory menorrhagias. Fresh **animal serum** or **antidiphtheritic serum** may be used by the rectum, or administered internally, in a little sweetened water, before the menstrual periods. P. Dalché (*N. Y. Med. Jour.*, Feb. 21, 1914).

Drugs are of little benefit, although **pituitrin** may be of value in young women. Dilatation and curettage finds its greatest value in diagnosis. The most satisfactory treatment, however, is by **radium** and the **X-ray**. They both have the effect of killing the follicles in the ovaries and thereby lessening the internal secretion. Radium is the more powerful in its effects; moreover, if the X-ray were continued for long, burns of the skin would result. In young girls with uterine insufficiency the writer places 50 mg. of radium in the uterus and leaves it from 4 to 12 hours. F. A. Pemberton (*Boston Med. and Surg. Jour.*, Apr. 11, 1918).

Diminution of both the duration and amount of menstruation noted in 53 out of 70 cases under **mammary extract**, 5 grains (0.3 Gm.) 3 times a day, with or without **thymus extract** in the same amount. The duration of administration was from 1 to 6 months. A. Jacoby (*N. Y. Med. Jour.*, Feb. 5, 1921).

The local measures may be subdivided into four classes: 1. Mechanical. 2. Surgical. 3. Electrical. 4. Röntgen therapy.

Very hot vaginal douches cause uterine contractions. The vaginal tampon or pack of non-absorbent cotton, lamb's wool, or gauze introduced through a bivalve speculum is effective. Enough gauze should be introduced to fill and distend the vagina from the cervix to the vaginal orifice. Intrauterine tampons of sterile gauze may be used if the cervix is sufficiently dilated.

Non-absorbent cotton recommended as tampon material. Refractory hemorrhages are arrested at once, and whereas with gauze tampons there is often seepage, this does not occur with the untreated cotton. The latter is wrapped in gauze to form a strip 5 to 10 cm. wide and 5 meters long, the gauze being tacked to the cotton with a few cross stitches. Barfurth (Münch. med. Woch., Aug. 20, 1920).

Intrauterine applications of iodine in solution; phenol pure, diluted or combined with iodine; creosote in solution are useful. Kelly has recommended fuming nitric acid as the best caustic, but it must be carefully applied through a cylindrical speculum, avoiding any excess of the acid. **Atmocausis** and **zestocausis**, introduced in Russia, have not been popular methods in America. The cauterization of the uterine cavity by these methods is difficult to regulate, is not entirely safe, and may obliterate the cavity.

Under surgical treatment **dilatation** and **curettement of the uterus** is a procedure which often enables one to make the diagnosis and cure the patient at the same time. It makes possible an exploration of the uterine cavity and by examination of the

scrapings reliable diagnostic evidence is secured. Curettement followed by **intra-uterine packing** is therapeutically efficient in interstitial endometritis, endometrial polyps or retained decidua material. Any gross lesion found should be removed by suitable measures.

Out of 111 cases in which **curettment** was done, according to Schickele and Keller, in 38 cases there was no recurrence of severe hemorrhage after the procedure. In 61 cases results were negative. In 13 cases **vaginal hysterectomy** had to be done for recurring hemorrhages.

In the hemorrhages of puberty and in young women with adnexal tumors, treatment of the abnormal ovaries is the only efficacious procedure. In hemorrhages from diffuse hyperplasia, which constituted a large proportion of the writer's 78 cases, destruction of ovarian tissue by the **X-ray** is the last resort. These cases, as well as those due to disturbed ovarian function, generally failed to respond to local treatment. On the other hand, hemorrhages due to chronic inflammations, atrophic mucous membrane in older women, and polyps were usually cured by local measures such as **curettement**, **cauterization**, etc. E. M. Fuss (Zent. f. Gyn., Feb. 21, 1925).

In cases of malignant or benign neoplasms **hysterectomy** is indicated. In inflammatory or infective processes or neoplasms involving tubes and ovaries the removal of these structures will be followed by cessation of hemorrhage.

The writer resorted to **splenectomy** in a case of thrombopenic menorrhagia. The X-ray exposures of the spleen and other measures tried 2 years had had no effect, but in 3 days after the splenectomy the thrombocytes had increased to 133,000, and during the ensuing 6 months, menstruation was normal and the girl in florid health. X-ray exposure of the ovaries has too many drawbacks for young girls, and

it acts only on the genital sphere, not warding off hemorrhages elsewhere. Halban (*Arch. f. Gyn.*, Apr. 16, 1923).

Electricity has its advocates, but it is not popular with the average gynecologist.

Some observers have considered **Röntgen treatment** the method of choice for the control of hemorrhage in patients approaching the menopause in whom carcinoma can be eliminated, but it is not the method in patients under 40 years of age.

In young women with excessive bleeding either at or between the periods and without tumor, **radium** in proper doses is the method of choice. Simple curettage, as a rule, does not permanently relieve these cases. A 50-mgm. radium tube, screened with $\frac{1}{2}$ mm. brass and enclosed in rubber tubing, is left in the uterus 4 to 12 hours, producing a temporary amenorrhea for about 3 months, after which the periods usually return normally. If for any reason radium cannot be used, the **X-rays** may be substituted, to be used with great care. Similar considerations apply in bleeding at or about the menopause where no tumor is present. A **preliminary curettage** may be done and the radium tube then allowed to remain 12 to 24 hours, as a rule inducing permanent amenorrhea and rendering further treatment unnecessary. With the X-rays the treatment in such cases is more prolonged, but the results are equally good. W. H. Schmidt (*Amer. Jour. of Electroth. and Rad.*, Nov., 1922).

X-rays applied to the spleen in 13 cases of hemorrhage of ovarian origin and in 12 caused by tumors of adnexa. The bleeding ceased within 1 hour after the application in a few cases, and in the others in from 1 to 3 days. Nürnberger (*Zent. f. Gyn.*, Jan. 6, 1923).

In 9 cases of uterine hemorrhage, a tube containing 100 mgm. of **radium bromide** was used. The length of exposure depends on the amount of radium used, the thickness of the

screening, the age of the patient, and the severity of the condition present. Varley (*Brit. Med. Jour.*, Feb. 23, 1924).

In menorrhagia and metrorrhagia of non-cancerous origin, **radium** should be applied in the uterus and not in the vagina, as the uterine walls are thicker, and consequently less exposed to injury. The author uses a rather small dose in the hemorrhages of the menopause, to maintain, even though feebly, the menstruation. The results are better with radium than with the X-rays, especially in menorrhagia. Halter (*Zent. f. Gyn.*, Sept. 13, 1924).

Of 200 cases of idiopathic uterine hemorrhage in which **radium** proved effective, 128 were at or near the menopause, and in these one exposure nearly always sufficed to establish amenorrhea. In a few instances recurrence took place. Of 14 cases requiring 2 exposures and 6 cases requiring 3 exposures before the menopause was induced, the most were in younger women. Fibroids were present as a complication in 30 of the 200 patients. Forsdike (*Brit. Med. Jour.*, Mar. 13, 1926).

At the Mayo Clinic, **radium** has given the best results.

In the Mayo Clinic **radium** is considered the treatment of choice in all cases of the menorrhagia of the menopause in which the presence of carcinoma is definitely excluded, either by history or by a diagnostic curettage, and in those cases not presenting a large, soft myoma which is apt to later undergo degeneration. It is also used in cases of profuse menstruation of the young woman (1) when there is a small submucous fibroid, (2) when no gross pathological condition is demonstrable, and (3) in cases presenting a large myoma in which there is a definite surgical risk. However, they have not entirely replaced myomectomy with radium for the treatment of myomas in the patients between the ages of 30 and 40. The dosage of radium is gauged by the age of the patient and by the presence or absence of a

tumor. In the young person without a demonstrable tumor and when it is desirable to continue menstruation, usually one application of 50 mg. of radium element for from four to six hours is used. In older persons in whom it is desirable to stop menstruation entirely, it has been found that an exposure of 50 mg. for from ten to twelve hours has brought about the desired results. In cases in which large dosage is used, menstruation is usually irregular for about two months and ceases entirely after the second or third month; following the lighter exposures, it becomes regular and normal in most instances in about two months. It is the custom in the Mayo Clinic not to repeat the treatment until an interval of three months has elapsed. Stacy (Minn. Med., Mar., 1919).

For its employment special training in Röntgen technique is necessary; but in order to determine the indications for such treatment, the gynecologist should make the differential diagnosis.

Kelly's 'utriculoplasty for uncontrollable uterine hemorrhage consists in a wedge-shaped excision of the greater part of the uterus, the base of the triangle being situated at the tubouterine junction, while the apex lies at the internal os. This excision leaves a strip of uterine mucosa on the lateral aspects of the uterine cavity which is continuous with that of the cervix below. The two moieties of the uterus are then united, first by a series of deep mattress sutures, then by a continuous superficial suture. V. Bonney (Lancet, May 13, 1911).

Hysterotomy is the ideal operation for diagnostic purposes, for uterine hemorrhage of doubtful origin, to differentiate between pregnancy and neoplasms resembling pregnancy, placenta previa, and toxemia of pregnancy, particularly the eclamptic type. The chief contraindication is infection, demonstrated or suspected.

J. B. Deaver (N. Y. Med. Jour., June 8, 1912).

MENOPAUSE.

This critical period in a woman's existence is characterized by a cessation of menstrual activity. The average age of the climacteric is between 40 and 45 years; but the time varies as widely as does the establishment of menstruation, and its cessation frequently occurs between 45 and 50 years.

It may be premature or retarded. The average duration of the menopause, or irregularities in menstruation, is about two and one-half years.

APPROXIMATE AGE OF MENOPAUSE.

Menses begun at 10th; should cease between 30th—52d						
"	"	"	11th	"	"	48th—50th
"	"	"	12th	"	"	46th—48th
"	"	"	13th	"	"	44th—46th
"	"	"	14th	"	"	42d—44th
"	"	"	15th	"	"	40th—42d
"	"	"	16th	"	"	38th—40th
"	"	"	17th	"	"	36th—38th
"	"	"	18th	"	"	34th—36th
"	"	"	19th	"	"	32d—34th
"	"	"	20th	"	"	30th—32d

The writer worked out the above table of "Approximate Ages" as a *practical working schedule* upon which to estimate the probable date of the menopause, as the age limit beyond which no woman should be allowed to go on menstruating without a thorough examination.

These figures are intended to represent the age limit in healthy women only, and vary widely from the averages collected by E. Krieger, which include all classes of women, regardless of general or pelvic disease.

Among 3700 patients seen by the writer in the gynecological departments of the Roosevelt Hospital, O. P. D., and the Northern Dispensary, there were 278 who had reached or passed the menopause, and, of these, 154 could recall their ages when menstruation began and ended. Of

the latter number, in 73, or 48 per cent., the menopause had been delayed beyond the "approximate age," including

3 cases of carcinoma uteri, an average of	7.0 years.
17 cases of flexion, version, or fixation, an average of	6.5 years.
15 cases of prolapsed uterus, vagina, and bladder, an average of	6.2 years.
4 cases of late recurrence, an average of	10.75 years.
39 cases, a total of 266 years, or an average of	7.00 years.

Of the same 3700 women, there were 484 over 35 years of age, 150 having passed the "approximate age" by a total of 837 years, or an average of 5.6 years, who were subject to one or another form of atypical menstruation amply justifying them in seeking relief from the burden of delayed menopause.

The menopause is "delayed" whenever menstruation is continued after the "approximate age," and this is always associated with uterine flexion, version, fixation, neoplasm, tubal disease, or syphilis, etc. A. E. Gallant (*Monthly Cyclo. and Med. Bull.*, Nov., 1910).

In a study of 800 menopause cases the writer found marked racial differences. Thus, Circassians have a later menopause than Indians; Indians later than Mongolians; dwellers in warm climates earlier than those in cold climates. Exceptions, however, were noted. The Austrian women cease menstruating 5 years earlier than the Germans, although of the same race. Persian women have a menopause 3 years earlier than Armenian women; the women of Southern Italy are later than those of the North. In the 708 cases studied the average age was from 45 to 50 years. Cases which started to menstruate either very early or very late ceased to menstruate early. This is contrary to the usual impression which supposes that very early cases continue later. Cases with extra pelvic pathology such as diabetes, nephritis, gout obesity have an average age of 47 years. Obesity often

coincides with early menopause and hypoactivity of the sex glands. Ovarian cysts induce early climacteric. Atrophic pelvic organs also induce it. The impression that early marriage produced a late menopause did not prove true; the later the marriage the later the menopause. Unmarried women have an early menopause. A number of pregnancies increase the menopause age. This is in accordance with theories of the influence of the Graafian follicle. The reproductive capacity of women is seldom used to the full extent and 34 years prove to be the average age of termination of fertility. The later the last pregnancy, the later the menopause. Profuse menstruation produces a later menopause with milder symptoms. Severe symptoms are usually attendant on an early menopause. Contrary to the usual belief a sudden menopause does not produce severe symptoms. The reverse is usually the case. K. I. Sanes (*Trans. Amer. Med. Assoc.; Med. Record*, Aug. 10, 1918).

SYMPTOMS.—During this period the patient is the subject usually of many discomforts, most of them due to vasomotor disturbances, such as flushes, sweating, cardiac palpitation, headache, melancholia, and neurasthenia. Occasionally the symptoms are more marked and the patient seeks relief for flushing of the face; a sensation of intense heat about the face and neck; palpitation of the heart; spells of weakness or prostration so great that she is compelled to frequently sit or even lie down; the flushings, etc., followed by free perspiration. With these there is more or less pronounced anemia, mental depression (sometimes almost amounting to melancholia), and broken slumber.

Some fortunate women, however, have an abrupt cessation of the men-

strual flow, and they glide away from the menstrual life easily and uneventfully.

As noted by Jung, there may be a general nervous irritability, alterations in personality, moodiness, and even increased sexual desire. In the normal subject the disturbances are mild and transitory. When serious and persistent, they may be looked upon as abnormal,—although some women may be castrated without much disturbance of function.

Psychoneurotic disturbances at the menopause usually have an organic basis, on which a superstructure of endocrin disorder has arisen. The individuals affected manifest more or less definite psychasthenic or psychopathic stigmata. Most of them are very "nervous" women, who manifest little power of resistance under the conditions of daily life. The origin of this defect lies in the regressive changes taking place in the sex glands. The glands involved are almost exclusively the ovaries and thyroid, and with either one it may be in the sense of increased or of diminished function. Treatment must take into account both these factors. R. F. Weiss (Therap. der Gegenwart, June, 1924).

In women at the menopause or with uterine myomas the writer observed an average increase of 20 mm. Hg in the blood-pressure. Cardiac enlargement coexisted in 15 to 20 per cent. and 40 per cent., respectively, of these 2 groups. The pressure is lowered by frequent hemorrhages. Surgical elimination of the ovarian function results in a primary reduction of blood-pressure, followed by a rise averaging 32 mm. systolic and 15 mm. diastolic. In X-ray treatment the result differs according to whether a small "ovarian" dosage is administered or deep radiation is given for malignancy. In the former case the amenorrhea induced is not attended with high blood-pressure, apparently because the ovarian internal secretion is not abolished, while in the latter, the blood-pressure rises and cardiac enlargement occurs. Strassman (Arch. f. Gyn., Sept. 9, 1925).

Where the menopause is delayed, such prolongation of the flow may be due to pathological conditions and investigation is indicated.

The fact that malignant disease of the uterus occurs so frequently during the fourth decade of life makes vigilance necessary during the menopausal period. Any postclimacteric hemorrhage should be viewed with suspicion and a most thorough study made of the individual case.

Like women, men go through a climacteric readjustment of tissues, though probably at a later age. At this time acute illness involves more than average risk. The counterpart of the ovarian changes is probably to be found in alterations in the prostate. Malignant growths often date from this period. Arteriosclerosis, interstitial nephritis, and diabetes form a group frequently seen in men between 55 and 63. G. Rankin (Brit. Med. Jour., Jan. 18, 1919).

Study of the effects of the X-ray on the ovaries in 700 cases of *artificial menopause*. The hot flushes are not due, as is generally believed, to a retention of toxins in the blood, but to a disturbance of the glandular apparatus. While they are attributed to loss of the ovarian function, the nature of the morbid process is still unexplained. The toxicity of the serum before or on the 1st day of menstruation, suggesting the accumulation of poisons about this period, has, however, been demonstrated by the experiments of Macht, which showed that blood serum obtained at this time inhibits the growth of plants. Bécclère (Bull. de l'Acad. de méd., Nov. 18, 1924).

TREATMENT.—Treatment of the menopause is indicated when the symptoms pass the physiological limits. It should be hygienic, psychotherapeutic, and symptomatic. **Rest**, with regulation of diet and bowels, is indi-

cated. Bromides and other nerve sedatives should be used sparingly.

The psychic disturbances should be dealt with sympathetically, but not too seriously, and patients should be impressed with the thought that their disturbances are not unnatural and will pass over before long, leaving them probably better emotionally, mentally, and physically than they were before. It should be made quite plain that the menopause is not a time of any special danger and that the healthy woman has nothing to fear from it. At the same time any deviation from health, either local or general, must be carefully investigated and treated, without being vaguely relegated to the limbo of incidents of the change of life. A course of **ammonium bromide**, in 10-grain (0.65 Gm.) doses, three times a day, combined with some bitter tonic, such as **tincture of cinchona**, is often very useful, both in checking flushes and in allaying nervous irritability. The taking of alcohol in any form should be discouraged, as it is peculiarly apt at this time to degenerate into the insidious practice of nipping. So many women at the menopause suffer from constipation and flatulence that special treatment should be directed to these points, and the tendency to obesity should be fought against by encouraging **exercise** and discouraging afternoon naps and sitting about all day. In some cases of artificial menopause the distressing flushes can be alleviated by the administration of **ovarian extract** in 5-grain (0.3 Gm.) doses, two or three times a day, continued for several days at a time. Giles (Lancet, Feb. 12, 1910).

Purely hygienic measures will in most cases largely overcome the various "congestive" symptoms at the climacteric. Physical **exercise**, especially walking, is very valuable; while walking in the open air is to be preferred, walking in the house, in conjunction with the household duties, is by no means useless. For

the prevention of insomnia the patient should be advised never to retire until at least two hours have elapsed since supper time and to walk around as much as possible during that time. The evening meal should be light and should not include any meat. The quantity of fluid taken should be reduced to half a pint. At other meals vegetables and fruit should chiefly be taken, especially during the "congestive" periods, though well-cooked white meats are also permissible. Skimmed milk often proves more acceptable than whole milk.

As derivative measures, **hot foot baths**, **dry cupping**, rubbing of the congested region with **turpentine** or **ammonia liniment**, careful **massage**, and the use of the **faradic current** are of chief value. Internal derivation by drugs such as aloes is to be avoided except in obstinate cases. Sedation by means of **bromides**, **monobromated camphor**, or **valerian** is useful in all cases where repeated nervous attacks occur. **Asafetida** may with advantage be given in the following combination, originally recommended by Debreyne:—

R Camphoræ,

Asafetidæãã gr. ij (0.1 Gm.).

Ext. belladonnæ

foliorum gr. ⅓ (0.02 Gm.).

Ft. in pil. no. j. Da tales no. lx.

Of these pills, from 2 to 6 may be administered daily; where the latter number is given, the amount of belladonna in each should preferably be reduced one-half. Of special value, especially in cases of artificially induced menopause, is the administration of dried **ovarian substance** in cachets or tablets each containing 0.1 Gm. (1½ grains); of these, 5 may be given daily. Plicque (Bull. méd., June 15, 1912).

The **extract of corpus luteum** has been of value in many cases, particularly in those of artificial menopause; but there is no special medicine that can be absolutely relied on at this period. This applies as well

to organotherapy as it does to other agents. **Ovarian extract** is recommended by some clinicians, **corpora lutea** by others; the possible inertness of some of the preparations on the market should not be overlooked.

In a case of premature menopause coming on after an attack of puerperal fever at 29, **pituitary extract** was begun after 10 or 12 years, and soon menstruation returned and general health improved. G. Jona (Gaz. degli Osped., Apr. 2, 1916).

There occurs in the majority of menopause cases a vacillating hypertension. The diastolic pressure is not elevated in proportion to the systolic, an increased pulse-pressure thus resulting. **Extract of corpora lutea** from animals in early gestation gradually restores the blood-pressure to normal. Carey Culbertson (Surg., Gyn. and Obst., Dec., 1916).

Extract of whole ovary gives quickest results in the natural menopause, next in the surgical menopause near the climacteric age, and lastly in the surgical menopause of young women. If the powder or tablets are used, the best results follow 5 grains (0.3 Gm.) 3 times a day, midway between meals, combined with $\frac{1}{40}$ grain (0.0015 Gm.) of **strychnine sulphate**. Nausea is common after oral use, and the writer prefers giving intramuscular injections deep into the deltoids, or better, intravenous injection. Reasonably fresh ampoules of 1 c.c. (16 minims), each containing 0.2 Gm. (3 grains) of the extract, are used. A series of 36 intramuscular injections usually suffices. For intravenous injections a boiled and cooled 3-c.c. syringe is used. In stout women the veins in the back of the hand are usually most accessible. The average patient shows no general reaction. Hirst (N. Y. Med. Jour., Oct. 5, 1921).

Some cases of prolongation of the menses beyond the usual limits are found to have cancer of the uterus. Symptoms due to lacerations, endometritis or pelvic inflammation demand proper treatment. Versions,

flexions, or prolapses require **pessaries**, preceded by **tampons** and **hydrotherapy**, or **surgical measures**. In the nervous type, **gland therapy** may be of value, and **valerian**, **strychnine** or **bromides** are useful. If no cause can be found, the uterus should be curetted for diagnostic examination. Syphilis may be the origin of the symptoms. Gilliam (Ky. Med. Jour., Mar., 1922).

In the hot flashes of the natural or artificially induced menopause, and sometimes the accompanying high blood-pressure, there is a reasonable prospect of benefit by the administration of **ovary**. J. Rogers (Med. Jour. and Rec., Jan. 2, 1924).

Thyroid gland is of distinct value when there are signs of hypothyroidia.

Where the menopause is associated with symptoms suggesting hyperthyroidism, the writer uses the **X-rays**. Whether amenorrhea has or has not yet occurred, he rays the ovaries repeatedly with doses sufficient to destroy the reproductive function while stimulating the internally secreting cells. In either case good results are reported, the symptoms usually disappearing, with reduction of high blood-pressure and improved general condition. Improvement of artificial menopause cases also occurred. Groedel (Munch. med. Woch., Mar. 24, 1922).

Following the menopause in a woman of 52, the author observed symptoms of exophthalmic goiter with kraurosis vulvæ and marked pruritus, at first general, then limited to the genital region. Almost complete recovery occurred under 3 **X-ray exposures of the thyroid**, **high-frequency current** to the vulva, and **ovary and pituitary** internally. The itching tended to recur upon temporary interruption of the ovarian treatment. Blamoutier (Paris méd., Oct. 14, 1922).

Ovarian grafting has been tried with apparent success, but further work will be required to place the procedure on a solid footing.

Ovarian grafting advocated in operations in which it is impossible to

leave an ovary, or part of an ovary, in the normal site during the reproductive period of life. The writer also retains a portion of the uterus, through the Bell-Beuttner operation, thus providing for continued menstruation. The ovary to be grafted, after its hard cortex has been shaved off, is divided by crisscross incisions into small parts held together by an underlying layer of tissue. A small incision is then made through the aponeurosis covering the rectus muscle, and a bed for the graft prepared by gently forcing compression forceps into the muscle and slowly separating the blades. By such grafting the menopause symptoms are abolished in 83 per cent. of cases, and do not reappear for some years. A period averaging 4 months elapses after the operation, however, before the graft begins to function. W. Blair Bell (Surg., Gyn. and Obst., Dec., 1925).

WILMER KRUSEN

AND

FRANK C. HAMMOND,
Philadelphia.

MENTAL DISEASES. See PSYCHOSES.

MENTHA.—Two varieties of mint, *mentha piperita* and *mentha viridis*, are official.

Mentha piperita, U. S. P., or peppermint, consists of leaves and tops of *Mentha piperita*, of the family Labiatae. It has an aromatic odor and taste, and contains a volatile oil, from which menthol is obtained.

Mentha viridis, U. S. P., or spearmint, consists of the leaves and tops of *Mentha spicata*, and also contains a volatile oil. It is somewhat less powerful than peppermint.

PREPARATIONS AND DOSE.—

Aqua menthae piperita, U. S. P. (peppermint water), contains 1:500 of the oil. Dose, 2 to 8 fluidrams (8 to 32 c.c.).

Oleum menthae piperita, U. S. P. (oil of peppermint), contains not less than 50 per cent. of total menthol. Dose, 1 to 5 minims (0.06 to 0.3 c.c.).

Spiritus menthae piperita, U. S. P. (spirit

of peppermint), contains 10 per cent. of the oil. Dose, 10 to 30 minims (0.3 to 2 c.c.).

Aqua menthae viridis, U. S. P. (spearmint water), contains 1:500 of the oil. Dose, 2 to 8 fluidrams (8 to 32 c.c.).

Oleum menthae viridis, U. S. P. (oil of spearmint). Dose, 1 to 5 minims (0.06 to 0.3 c.c.).

Spiritus menthae viridis, U. S. P. (spirit of spearmint), contains 10 per cent. of the oil. Dose, 10 to 30 minims (0.3 to 2 c.c.).

THERAPEUTICS.—The bruised fresh leaves of peppermint are useful domestic remedies for the relief of **colic**, **sick headache**, **nausea**, etc. Peppermint water is used as a flavoring agent and to lessen the griping effect of certain remedies. It is a popular remedy for **colic** and **flatulence** in infants, especially when combined with a small dose of sodium bicarbonate ("soda mint").

The spirit may be used for the same purpose in adults. The oil may be painted over the course of the nerves in **neuralgia** and **myalgia**, and over the painful joints in **arthralgia** and **chronic gout**. Evaporation should be prevented by covering with oiled muslin. In **dental caries** it acts both as antiseptic and analgesic. In **acute rheumatism** the oil may be applied to the painful joints and covered with cotton and oiled muslin. W. and S.

MENTHOL.—Menthol (mint camphor) $[C_{10}H_{19}(CH_3)(OH)(C_3H_7)]$ is a stearopten, or secondary alcohol, obtained from the essential oil of *Mentha piperita* or other mint oils. It occurs in colorless, acicular or prismatic, glossy crystals having a strong peppermint odor. It is soluble in alcohol, ether, carbon bisulphide, oils, and acetic acid, and is slightly soluble in water. It melts at 109.4° F. (43° C.) and volatilizes slowly at ordinary temperatures. It can be fused or compressed into cones or pencils. Chinese and Japanese oils of peppermint are richer in menthol than the official oil.

PREPARATIONS AND DOSES.—

Menthol, U. S. P. (menthol), is the only pharmacopoeial preparation. Dose, ½ to 5 grains (0.03 to 0.3 Gm.).

Menthol camphoratum, N. F. (camphormenthol), is an oily fluid produced by

trituration equal parts of camphor and menthol. Used externally.

Various unofficial camphor combinations, all antiseptic and analgesic, have come into use:—

Coryfin (koryfin) is the ethylglycolic acid ester of menthol; it occurs as a limpid, colorless oil, having a faint menthol odor. Dose, 3 or 4 drops on sugar.

Loeffler's solution, mentholated, consists of menthol, 10 parts; toluol, 34; liquor ferri chloridi, 4; absolute alcohol, 60.

Menthol-eucalyptol consists of menthol, 10 parts; eucalyptol, 20; oleum ricini, 100. Dose, 30 minims (2 c.c.), by intramuscular injection.

Menthol-iodol consists of menthol, 1 part; iodol, 99. It occurs as a powder or can be molded into cones or pencils. Used externally.

Menthol-phenol consists of menthol, 3 parts; phenol, 1; melted together. Used externally.

Menthospirin is an acetylsalicylic acid ester of menthol; it occurs as a light-yellow fluid. Dose, 4 grains (0.25 Gm.) in capsule.

Validol (menthol valerate), containing 30 per cent. of free menthol, occurs as a colorless liquid of the consistency of glycerin, with a mild, pleasant odor, and soluble in alcohol, ether, chloroform, and oils. Dose, 10 to 20 drops on sugar or in sweetened wine, as nerve sedative, carminative, and stomachic.

Validol camphoratum, a 10 per cent. solution of camphor in validol. Dose, 10 to 20 drops on sugar or in wine. In odontalgia may be applied to the pulp or inserted on cotton.

PHYSIOLOGICAL ACTION.—Menthol in small doses tends, like camphor, to stimulate the heart. Toxic doses depress it, and also paralyze the central nervous system.

In the alimentary canal small doses of menthol cause slight local irritation; large doses, vomiting.

Externally, menthol depresses the nerves of pain and tactile sensation, and stimulates those of cold and heat sensations. These effects, according to the researches of Joteyko, do not set in simultaneously, but appear in the following

order: 1. Pain. 2. Cold. 3. Touch. 4. Heat. The characteristic cold sensation produced is not associated with a fall in local temperature,—the superficial vessels being in fact dilated,—but to the excitation of the nerves of cold sense. It is only when the drug is very freely used that the heat nerves are acted upon and a sensation of heat and formication results (Joteyko).

THERAPEUTICS.—Menthol may be used in doses of from 3 to 5 grains (0.2 to 0.3 Gm.) in capsules for the relief of **nervous dyspepsia** and **diarrhea**. Validol (10 drops) and menthol in doses of 1 or 2 grains (0.06 or 0.13 Gm.) are useful as sedatives in **gastralgia**, and likewise in **flatulence** in general, in the **indigestion** of **chlorosis** and of **early phthisis**, in **gastric neurasthenia**, in the **vomiting of pregnancy**, and in cases of **gastric ulcer** and even of **gastric cancer**. They are, however, contraindicated in the presence of acute inflammation of the stomach or hemorrhage.

In **hysteria** and **epilepsy** validol exerts a sedative action. Used externally, like menthol, coryfin, or menthophenol, it affords relief in painful and **neuralgic** affections, **headache**, **toothache**, **insect bites**, and **pruritus**, being rubbed or painted over the affected parts, or applied in alcoholic solution or in an ointment. One dram (4 Gm.) of menthol may be dissolved in 4 ounces (125 c.c.) of soap liniment for external use. Menthospirin and camphor-menthol may be similarly used, applied with a camel-hair pencil. The pain and itching of **herpes zoster** and **urticaria** can frequently be relieved by the application of a 5 per cent. ointment of menthol.

Menthol is given internally for the relief of **hemicrania**, **intraorbital neuralgia**, **cephalalgia**, **sciatica**, and **rheumatism** in doses of from 4 to 10 grains (0.25 to 0.65 Gm.).

Menthol, or camphor-menthol, may be used as a depletant to the mucous membranes of the nose or throat. It causes a contraction of the local blood-vessels which, unlike the action of cocaine, is not followed by increased dilatation. Dissolved in oil (1:80), or in liquid petrolatum (1:100), it may be used in a spray

for the relief of **acute coryza** and the nasal symptoms of **hay fever**. A mixture of menthol and ammonium carbonate may be used for the same purpose, inhaled from a wide-mouthed bottle or an inhaling tube.

Leroux, Lublinski, Mayet, and others have observed alarming dyspnea and suffocation follow the use of menthol in the noses and throats of infants. They advise its omission from infantile therapeutics.

In **ozena**, **hypertrophic rhinitis**, **pharyngitis**, etc., camphor-menthol, menthol-iodol, and menthol-phenol will yield good results, used in a spray of a 1 to 4 per cent. solution in liquid petrolatum. Inhalations of menthol volatilized by the addition of hot water have been used with advantage in **bronchial asthma**.

In **diphtheria** Loeffler's mentholized solution is used to remove and prevent the formation of false membrane. It is applied on a cotton pledget every three hours to the mucous membrane, previously dried off with cotton.

Intralaryngeal injections of 10 or 15 per cent. solutions of menthol have been used in **pulmonary tuberculosis** and in **ulcerations of the larynx**. Deep injections into the gluteal muscles of menthol-eucalyptol have been used with benefit in lung affections marked with abundant or putrid expectoration, and in pulmonary phthisis.

The menthol preparations have found favor in the treatment of painful **wounds**, especially in the case of menthol-iodol, which is odorless and non-irritating and may be used as a dusting powder or in an ointment.

Mentholized oil (10 to 15 per cent.) has been recommended in the treatment of **furuncle** of the **external auditory canal** and of diffuse swelling of the wall of that canal. In **chronic otitis media** mentholized oil (5 to 10 per cent.) is valuable as a mild antiseptic for the interior of the tympanum.

Equal parts of chloral and menthol form, upon trituration, an oily substance which is mildly counterirritant and anesthetic.

Squibb's solution for local anesthesia, which is used in an ordinary hand spray, consists of menthol, 2 parts;

chloroform, 20; ether, 31. The effect lasts five minutes.

Mentholization of the air passages before, during, and after etherization has been suggested by Briggs, who asserts that anesthesia is more rapidly induced, with absence of cough, suffocation, and preliminary excitement, and less post-operative nausea and vomiting. One fluidram (4 c.c.) of peppermint oil, or a 50 per cent. alcoholic solution of menthol, is poured on to the inhaler and, after 6 good inhalations, etherization is begun.

W. and S.

MERCURY.—Mercury, hydrargyrum, or quicksilver is a lustrous, bluish-silver-white liquid metal, which, though occasionally found in its pure state, is usually obtained from native chloride or sulphide. It is also found in amalgamation with silver. The sulphide, called native cinnabar, is mainly obtained in the mines of Almaden, Spain, and of New Almaden, near San Jose, California. The various processes through which it is isolated are all based upon distillation.

Mercury is devoid of odor or taste. Its specific gravity is 13.535 times that of water. At -39.4° C. (-38.9° F.) it congeals into a malleable solid, and when exposed to a temperature of 357° C. (675° F.) boils, turning into a colorless vapor. It volatilizes spontaneously to a less extent, however, at all ordinary temperatures. It is soluble in nitric acid and in boiling sulphuric acid.

PREPARATIONS AND DOSE.

—The official preparations of mercury may appropriately be classified in several distinct groups, as follows:

A. Metallic Mercury.

Hydrargyrum, U. S. P. (mercury) [Hg], is not less than 99.5 per cent. pure.

Hydrargyrum cum creta, U. S. P. (mercury with chalk; gray powder),

made from 38 parts of mercury, 10 parts of honey, 57 parts of prepared chalk, and a small amount of water. The finished product contains 38 per cent. of mercury, and occurs as a light-gray, smooth powder with a slightly sweetish taste. Dose, in adults, 4 grains (0.25 Gm.); in children, $\frac{1}{2}$ to 2 grains (0.03 to 0.12 Gm.).

Massa hydrargyri, U. S. P. (mass of mercury; blue mass), made from 33 parts of mercury, 1 part of oleate of mercury, 32 parts of honey of rose, 10 parts of licorice, 15 parts of althea, and 9 parts of glycerin. Trituration is continued until the mercury (33 per cent.) globules are no longer visible under a microscope magnifying 10 diameters. Dose, 1 to 10 grains (0.06 to 0.6 Gm.); official average dose, 5 grains (0.3 Gm.).

Unguentum hydrargyri fortius, U. S. P. (stronger mercurial ointment), made from 50 parts of mercury, 2 parts of oleate of mercury, 23 parts of prepared suet, and 25 parts of benzoinated lard. Trituration is continued to the same point as for blue mass. Used externally.

Unguentum hydrargyri mite, U. S. P. (mild mercurial ointment; blue ointment), made by mixing 60 parts of stronger mercurial ointment with 20 parts each of petrolatum and simple ointment. The preparation contains 29 to 31 per cent. of mercury. Used externally.

Emplastrum hydrargyri, U. S. P. VIII (mercurial plaster), made by trituration of 30 parts of mercury with 1 part of oleate of mercury, 10 parts of hydrous wool-fat, and 59 parts of lead plaster. Used externally.

B. Oxides of Mercury.

Hydrargyri oxidum flavum, U. S. P. (yellow mercuric oxide; yellow pre-

cipitate) [HgO], made by precipitation of 10 parts of corrosive mercuric chloride, dissolved in 100 parts of distilled water, with 4 parts of sodium hydroxide, dissolved in 100 parts of distilled water. It occurs as an orange-yellow, heavy, impalpable powder, with a somewhat metallic taste, darkening on exposure to light, practically insoluble in water, insoluble in alcohol, but soluble in diluted hydrochloric or nitric acid, forming colorless solutions. Used externally.

Oleatum hydrargyri, U. S. P. (oleate of mercury; mercuric oleate), made by mixing 25 parts of yellow mercuric oxide with 75 parts of oleic acid, warming to a temperature not exceeding 50° C., and continuing the heat, with frequent stirring, until the mercuric oxide is dissolved; enough oleic acid is then added to make 100 parts. It contains 25 per cent. yellow mercuric oxide, is of firm butter consistence, and of a yellow color. The 5, 10, and 20 per cent. oleates of mercury can be prepared from the official (U. S. P.) by diluting the same with oleic acid.

Unguentum hydrargyri oxidi flavi, U. S. P. (ointment of yellow mercuric oxide), made by trituration of 1 part of the yellow oxide with 1 part of liquid petrolatum until the mixture is smooth, adding 10 parts of hydrous wool-fat in divided portions, and incorporating the mixture thoroughly with 88 parts of petrolatum. Used externally.

Hydrargyri oxidum rubrum, N. F. (red mercuric oxide; red precipitate) [HgO], occurring in heavy, orange-red scales or powder, with a somewhat metallic taste, with the same solubilities as the yellow oxide. Used externally.

Unguentum hydrargyri oxidi rubri, N. F. (ointment of red mercuric oxide), by trituration of 10 parts of red oxide with 10 parts of water and 40 parts each of hydrous wool-fat and petrolatum. Used externally.

C. Ammoniated Mercury.

Hydrargyrum ammoniatum, U. S. P. (ammoniated mercury; white precipitate) $[\text{HgNH}_2\text{Cl}]$, made by pouring a 5 per cent. solution of corrosive mercuric chloride into ammonia water, and collecting, washing, and drying the precipitate. It should contain not less than 78 per cent. nor more than 80 per cent. of metallic mercury and occurs in white pieces or powder, with an earthy and afterward styptic and metallic taste, insoluble in water or alcohol, but readily soluble in warm mineral acids and in a cold solution of ammonium carbonate. It is decomposed on prolonged washing with water. Used externally.

Unguentum hydrargyri ammoniati, U. S. P. (ointment of ammoniated mercury), made from 10 parts each of ammoniated mercury and liquid petrolatum and 40 parts each of hydrous wool-fat and white petrolatum. Used externally.

D. Nitrates of Mercury.

Liquor hydrargyri nitratis, N. F. IV (solution of mercuric nitrate), made from 40 parts of red mercuric oxide, 45 parts of nitric acid, and 15 parts of distilled water. It contains about 60 per cent. of mercuric nitrate $[\text{Hg}(\text{NO}_3)_2]$ and 11 per cent. of free nitric acid, and occurs as a clear, nearly colorless, heavy liquid, with a faint odor of nitric acid. Used externally.

Unguentum hydrargyri nitratis, N. F. (ointment of mercuric nitrate; citrine

ointment), made by warming 76 parts of lard until melted, adding 7 parts of nitric acid and continuing the heat until the reaction is complete, cooling and stirring, dissolving 7 parts of mercury in 10.5 parts of nitric acid, and mixing this with the previously prepared lard. Used externally.

E. Iodides of Mercury.

Hydrargyri iodidum flavum, U. S. P. (yellow mercurous iodide; green iodide of mercury; mercury protiodide or protoiodide) $[\text{HgI}]$, occurs as a bright-yellow, amorphous, tasteless powder, becoming greenish on exposure to light in proportion as it undergoes decomposition into mercury and mercuric iodide. It is practically insoluble in water, and wholly insoluble in alcohol or ether. Dose, $\frac{1}{8}$ to $\frac{1}{2}$ grain (0.008 to 0.03 Gm.); official average dose, $\frac{1}{6}$ grain (0.01 Gm.).

Hydrargyri iodidum rubrum, U. S. P. (red mercuric iodide; mercury biniodide) $[\text{HgI}_2]$, occurs as a scarlet-red, amorphous, tasteless powder, practically insoluble in water. One Gm. is soluble in 115 c.c. of alcohol and in 120 c.c. of ether; it is also soluble in solutions of the iodides, mercuric chloride, sodium thiosulphate, and hot solutions of the alkali chlorides. Dose, $\frac{1}{32}$ to $\frac{1}{8}$ grain (0.002 to 0.008 Gm.); official average dose, $\frac{1}{15}$ grain (0.004 Gm.).

Liquor arseni et hydrargyri iodidi, U. S. P. (solution of arsenous and mercuric iodide; Donovan's solution). For composition, see ARSENIC. Dose, $1\frac{1}{2}$ minims (0.1 c.c.).

Liquor hydrargyri et potassii iodidi, N. F. IV (solution of mercuric and potassium iodides; Channing's solution), contains 1 per cent. of red mercuric iodide and 0.8 per cent. of potassium iodide. Dose, 3 minims 0.2 c.c.).

F. Chlorides of Mercury.

Hydrargyri chloridum corrosivum, U. S. P. (corrosive mercuric chloride; mercuric chloride; bichloride of mercury; corrosive sublimate) [HgCl_2], occurring in heavy crystals or crystalline masses, with an acrid and persistent metallic taste. One Gm. is soluble in 13.5 c.c. of water, in 3.8 c.c. of alcohol, and in about 12 c.c. of glycerin. Dose, $\frac{1}{100}$ to $\frac{1}{3}$ grain (0.0006 to 0.02 Gm.); official average dose, $\frac{1}{15}$ grain (0.004 Gm.).

Hydrargyri chloridum mite, U. S. P. (mild mercurous chloride; mercurous chloride; calomel) [HgCl], occurring as a heavy, white, impalpable powder, becoming yellowish on trituration under strong pressure, tasteless, and insoluble in water, alcohol, ether, or cold dilute acids. Dose, $\frac{1}{4}$ to 10 grains (0.015 to 0.6 Gm.); official laxative dose, $2\frac{1}{2}$ grains (0.15 Gm.).

Pilula hydrargyri chloridi mitis composita, U. S. P. ("compound cathartic pills"), each containing $1\frac{1}{3}$ grains (0.08 Gm.) of compound extract of colocynth, 1 grain (0.06 Gm.) of calomel, $\frac{1}{3}$ grain (0.02 Gm.) of resin of jalap, and $\frac{1}{4}$ grain (0.015 Gm.) of gamboge. Dose, 2 pills.

Toxotabellæ hydrargyri chloridi corrosivi, U. S. P. (poison tablets of corrosive mercuric chloride; bichloride tablets). Tablets of an angular shape, each with the word "POISON" and the skull and crossbones distinctly stamped on it, and each containing 0.45 to 0.55 Gm. of mercuric chloride, the remainder being chiefly sodium chloride or ammonium chloride. The tablets are colored blue, preferably with sodium indigotinsulphonate. Used externally.

G. Salicylate of Mercury.

Hydrargyri salicylas, U. S. P. (mercuric salicylate) occurring as a white,

slightly yellowish or slightly pinkish powder, containing 54 to 59.5 per cent. of mercury. It is practically insoluble in water or alcohol, but dissolves in a warm solution of sodium chloride and in solutions of the fixed alkalies or their carbonates, with the formation of double salts. Dose, $\frac{1}{50}$ to 1 grain (0.0012 to 0.06 Gm.). Official average dose (intramuscular), 1 grain (0.06 Gm.), twice a week.

Lotio flava, N. F. (yellow wash), made by dissolving 3 parts of mercuric chloride in 35 parts of boiling water and adding lime-water to make 1000 parts. Used externally.

Lotio nigra, N. F. (black wash), made by triturating 8.75 parts of mild mercurous chloride with 15 parts of water and adding enough lime-water to make 1000 parts. Used externally.

In addition to the above preparations, the following unofficial combinations of mercury are in use:—

Mercuric benzoate [$\text{Hg}(\text{C}_7\text{H}_5\text{O}_2)_2 + \text{H}_2\text{O}$], occurring in white crystals, insoluble in water, slightly soluble in alcohol, and easily soluble in solutions of sodium chloride or ammonium benzoate. Dose, $\frac{1}{32}$ to $\frac{1}{8}$ grain (0.002 to 0.012 Gm.); may be given hypodermically.

Mercuric cyanide [$\text{Hg}(\text{CN})_2$], occurring in colorless prisms with a bitter taste, darkened by light, and soluble in water and alcohol. Less irritating than mercuric chloride. Dose, $\frac{1}{32}$ to $\frac{1}{8}$ grain (0.002 to 0.012 Gm.). Also used externally in 0.01 per cent. solution.

Mercuric oxycyanide [$\text{HgO.Hg}(\text{CN})_2$], occurring as a white, crystalline powder, soluble in hot water. Used externally as antiseptic in 0.2 to 2 per cent. solution.

Mercury subsulphate (basic mer-

curic sulphate; turpeth mineral) [$\text{HgSO}_4 \cdot 2\text{HgO}$], occurring as a heavy, lemon-yellow powder, almost tasteless, partially soluble in water, and soluble in acids. Dose, as alterative, $\frac{1}{4}$ to $\frac{1}{2}$ grain (0.015 to 0.03 Gm.); as emetic, $1\frac{1}{2}$ to 3 gr. (0.1 to 0.2 Gm.).

Mercuric succinimide (or imido-succinate) [$\text{Hg}(\text{C}_2\text{H}_4 \cdot \text{C}_2\text{O}_2 \cdot \text{N})_2$], occurring as a white, crystalline powder, soluble in 50 or 75 parts of cold water, and in 25 parts of water with the aid of heat. Dose (hypodermically), $\frac{1}{8}$ to $\frac{1}{3}$ grain (0.012 to 0.2 Gm.).

Flumerin, the disodium salt of hydroxymercurifluorescein, occurring as a dark red powder with greenish iridescence, freely soluble in water. Injected intravenously in syphilis. Dose, 2 to 5 mgm. ($\frac{1}{32}$ to $\frac{1}{13}$ grain) per kilo. (2.2 lbs.) of body weight.

Meroxyl, the sodium salt of dihydroxymercuri-dihydroxybenzo-phenone-sulphonic acid, forming a pale brownish-pink solution with green fluorescence. Found by Young *et al.* to be 4 to 5 times as effective against the gonococcus as mercurochrome. Injected 4 or 5 times a day in 0.5 per cent. solution.

Mercurochrome and Metaphen, see special sections at the end of this article.

Novasurol, see separate article, Vol. VII.

INCOMPATIBILITIES. — Mercuric chloride is incompatible with alkaloids, alkalies, lime-water, and soap. A small quantity of green soap is sufficient to destroy a large basinful of bichloride solution. Carbonates, silicates, and sulphates, such as occur in natural waters, also decompose mercuric chloride (Bastedo).

MODES OF ADMINISTRATION.—The several methods of administration of mercury, particularly

in syphilis, may be enumerated as follows: (1) oral; (2) intramuscular; (3) inunction; (4) intravenous; (5) by the respiratory tract—(a) mask, (b) chest protector, (c) plaster; (6) suppositories; (7) fumigation; (8) baths. The last 4 of these methods are relatively inferior and seldom used.

By mouth the preparations generally used are the protiodide, the biniodide, the bichloride in admixture with potassium iodide (forming the biniodide), and in children mercury with chalk. The disadvantage of oral administration is the special tendency to gastroenteric disturbance upon prolonged treatment.

Addition of glycerin, according to Martinet, will keep mercurial pills from drying up. He combines opium and guaiac with the mercury and glycerin, to increase intestinal tolerance for the mercury, using $\frac{1}{6}$ grain (0.01 Gm.) of bichloride of mercury, $\frac{1}{3}$ grain (0.02 Gm.) of extract of opium, and $\frac{2}{3}$ grain (0.04 Gm.) of extract of guaiac, with glycerin enough to make 1 pill. Two or 3 pills are ordered daily, before or during meals; the dose may be increased to 6 a day, if required and tolerated.

For the routine treatment of syphilis intramuscular injection is by many considered best, being most convenient, cleanly, and exact. Injections of mercury bichloride are, however, decidedly painful and irritating to the tissues, though the pain may be diminished by addition of sodium chloride or some local anesthetic to the solution. Mercuric salicylate acts less harshly on the tissues than the chloride, not being followed usually by scarring or abscesses (Montgomery). It is generally given in oil or wool-fat in 10 to 20 per cent. strength and in doses of $\frac{1}{2}$ to $1\frac{1}{2}$

grains (0.03 to 0.1 Gm.), injected into the buttock twice a week. The more soluble mercuric benzoate is also a good preparation, though it is more rapidly absorbed and must therefore be given at shorter intervals, *e.g.*, on alternate days. Other relatively non-irritant preparations of mercury suitable for intramuscular injection are the cyanide, the succinimide, and the albuminate (kept in solution by means of sodium chloride or carbonate). The average daily dose of such preparations is 1 c.c. (16 minims) of a 1 per cent. solution. The biniodide, dissolved in 3 per cent. sodium iodide solution, is also sometimes used. Injections of insoluble preparations suspended in oil, *e.g.*, calomel, yellow oxide, or metallic mercury (as a 50 per cent. suspension in hydrated wool-fat), are also in use, though with such preparations there is some danger of temporary non-absorption, with later possibly sudden absorption of a large quantity, resulting in marked mercurial intoxication. The object in using such preparations is to form a "depot" from which the drug is gradually absorbed, thus dispensing with injections more frequent than every 5 to 7 days. Proper depth of injection—always well through the fatty tissues—is an important point in the avoidance of local irritative or necrotic effects. The most slowly absorbed type of preparation is gray oil (*oleum cinereum*), a 40 per cent. suspension of metallic mercury in oil; dose, 0.25 c.c. (4 minims), administered weekly for 5 weeks.

Studying by means of the X-rays the absorption of various mercurials given intramuscularly, the author found gray oil entirely unabsorbed on prolonged observation; he advises against

its use. Calomel injections are also dangerous. Mercuric salicylate was completely absorbed from the gluteal muscles in an average of 4 days, and is to be preferred. Cole (*Jour. Amer. Med. Assoc.*, Dec. 4, 1920).

The inunction method, though in general highly efficient, is less precise than the intramuscular use of soluble mercurials, and, besides soiling the clothing, is apt to irritate the skin. The procedure consists in rubbing thoroughly 10 to 30 grains (0.6 to 2 Gm.) of the stronger mercurial ointment, frequently diluted one-half, into the inner surface of the thighs, on the chest, the back, and the abdomen, daily or on alternate days. The oleate of mercury, or the ointment of ammoniated mercury (more irritating), is also at times employed. Previous free diaphoresis hastens the absorption of the mercury.

Fifty per cent. mercurial ointment, undiluted, favored for use in children; it need not be repeated oftener than twice a week. Calomel ointment is less rapidly absorbed, and a higher concentration is required. Mercuric salicylate in oil should be injected twice instead of once weekly. Mercuric chloride hypodermically should not be used in children, often causing albuminuria. Calomel by mouth is absorbed and eliminated slowly; giving it at intervals of several days should suffice, thus avoiding diarrhea. Gray powder is absorbed to a small degree and eliminated rapidly, so that large doses daily would seem necessary. Ramsey and Groebner (*Amer. Jour. Dis. of Childr.*, Sept., 1920).

Uncleanliness, folliculitis and the fear of discovery, the objections to the inunction method, are obviated by thoroughly removing the residue of ointment on the skin after 30 minutes' rubbing with the official ointment by the free use of benzine and cotton. This procedure was successfully applied in 44 cases. The writers believe

Report of experiments showing that mercury is highly toxic to the heart, causing various irregularities, such as heart-block, delirium cordis, and finally paralysis. In the turtle heart, perfusion with even 1:10,000,000 of mercury at times sufficed to bring on delirium cordis. Mercurochrome intravenously was better tolerated in mammals than mercury acetate, succinate, or benzoate. In several experiments the onset of delirium cordis and heart-block produced by mercury was hastened by the injection of epinephrin. Mercury in the small intestine induced symptoms sooner than when given intramuscularly. Salant (Jour. Amer. Med. Assoc., Dec. 16, 1922).

Alimentary Tract.—Mercurials appear to exert a rather special action on the salivary and oral mucous glands, causing, when pushed, profuse discharge of a mercury-laden, irritating saliva with a metallic taste, and a stomatitis which may eventuate in the formation of ulcers.

The stomach and small intestine, with the contained digestive ferments, are relatively little influenced by mercury. The cecum and colon, on the other hand, appear to be very susceptible to its action and respond quickly to ingestion of an excess of the element by hyperemia and swelling of the mucous membrane, followed by necrotic changes, ulcer formation, dysenteric symptoms, and, possibly, perforation.

Mercurials ingested in small amounts induce purgation, presumably by direct irritation of the intestinal walls. The insoluble preparations are thus employed, as irritation of the stomach is thereby avoided, and the local effects are not developed until the drug reaches the intestinal epithelia, for which it has special affinity, partial dissolution of the mercurial preparation being then probably ef-

fected. The green stools not infrequently associated with calomel purgation are believed to arise not through an action of the drug in increasing the flow of bile,—which effect has been shown not to occur,—but through its antiputrefactive action, the bile being, therefore, preserved from bacterial decomposition, as well as hastened in its passage through the alimentary tract.

Kidneys.—Diuresis is a frequent effect of moderate doses of calomel, especially in cases of cardiac dropsy. The extent of diuresis tends to vary inversely with that of purgation. Wellander has shown that the elimination of mercury through the kidneys is attended by more or less temporary irritation when the drug is administered for some time.

Fürbringer asserts that syphilitics under mercurial treatment frequently develop nephritis, from which, however, recovery tends always to occur upon cessation of the drug.

Intravenous injections of mercury in rabbits in amounts as low as 0.00002 Gm. ($\frac{1}{3000}$ grain) per kilo. of body weight caused well-defined microscopic pathologic changes in the kidney and liver in 5 minutes. Menten (Jour. of Med. Res., June-July, 1922).

According to Meyer, calomel, by reason of the traces of mercury ions given off by it in the bowel, causes the intestinal epithelium with which it comes in contact to swell, thereby hindering the water in the bowel from entering the lymph and blood, and thus forcing edematous tissues, such as are present in cases in which calomel is used as diuretic, to give up their excess of water to the anhydremic blood.

Albumin and casts are often to be found in the urine of mercury-treated

syphilitic patients. According to some, these findings are less frequent in those given injections of soluble mercurials than in those given insoluble salts subcutaneously or treated by inunction.

The evident renal irritant property of mercurials would tend to suggest that the diuretic action of calomel is due to direct irritation of the kidney cells. Some believe its effect, however, due rather to the relief of splanchnic—including renal—congestion through the removal of fluid by the bowels consequent on purging.

In toxic amounts mercurials lead to changes in the renal tissues, anuria frequently resulting. These changes consist in necrosis of the epithelium of the convoluted tubules, accompanied by diffuse congestion of the organ and, if the process be long enough continued, by degeneration of the glomeruli and fibrosis. A peculiar feature is the not infrequent deposition of calcium phosphate in the injured convoluted tubules.

Blood.—Wilbouchewitch showed that large doses of mercury caused a reduction in the number of red blood-corpuscles, while small doses prevented their destruction. When, however, small doses were administered during too prolonged a period, anemia was again observed. Keyes, in a series of experiments, further demonstrated that small doses of mercury not only arrest the destruction of corpuscles due to syphilis, but actually cause an increase, which steadily progresses until the normal is attained.

Large doses, on the contrary, exert an opposite influence, being distinctly debilitating. Robin, acting on these conclusions, found that in syphilitic or non-syphilitic

subjects, and in whatever way administered, mercury always caused an increase of blood-corpuscles, provided an intercurrent gastric disorder were not present or the untoward effects of the drug—salivation, etc.—were not produced. The onset of these disorders marked the beginning of an hypoglobulia, or decrease in the number of corpuscles. Kupferwasser found that in the blood of healthy subjects the proportion of young leucocytes is considerably increased and that of old leucocytes considerably diminished by mercury. The blood of syphilitics, on the other hand, reacts to mercury by a considerable diminution in the proportion of young and a corresponding increase in that of old leucocytes. This reaction is independent of the stage of the disease, and takes place whether there are at the time syphilitic manifestations or not, and also whether the patient has or has not previously been subjected to treatment by mercury and iodides. Those who have undergone treatment by mercury within four months before the blood examination form the only exception to this rule. In such cases the reaction of syphilitic is replaced by that of healthy blood, possibly because the patient still retains a considerable quantity of mercury, or because under its influence the disease has become so attenuated that the blood gives a normal reaction.

Older observers had noted a diminution of fibrin, and as a result an abnormal fluidity of the blood that predisposed to hemorrhage. Lowering of the rate and tension of the pulse and of the temperature, sometimes to the extent of nearly 2° were also noted,—all evidence that the rem-

edy had been administered in injudicious doses in these cases.

The observations of Krohl tend to show that mercury in small doses has, to some extent, the property of conferring immunity against septic processes.

Small quantities of mercury accelerate and accentuate immune serum hemolysis *in vitro*, so that possible fixation of complement may be missed. Corrosive sublimate, injected subcutaneously, will likewise appear in the blood of the living rabbit in sufficient strength to inhibit complement fixation. Thus, caution must be exercised in interpreting the disappearance of a previously positive Wassermann reaction in a patient under mercurial treatment. This disappearance may be due simply to the fact that enough mercury is circulating in the patient's blood to inhibit the reaction. Epstein and Pribram (Zeit. f. exper. Path. u. Therap., Bd. vii, S. 549, 1909).

The author observed that patients taking a course of mercurial treatment seemed to be peculiarly resistant to ordinary infectious diseases, especially to epidemics of cholera. This fact and others suggested that mercury might have an action on the blood, rendering it immune to septic processes, and the author's experiments with 77 rabbits apparently confirm this. Rabbits injected with mercuric benzoate bore without harm the injection of serum from the blood of a woman who had died of puerperal fever, or injection of pure cultures of streptococci. The doses of mercury given were small; a series of injections of 0.0015 Gm. ($\frac{1}{42}$ grain) to 1 kg. of body weight rendered the animal non-susceptible to infection with streptococci. A shorter series of injections with a slightly larger dose answers the same purpose. The drug showed such efficiency that the author applied the same treatment to patients threatened with septic processes, and he reports

a few illustrative cases. Once developed, the septic affection is not modified by the small doses which he recommends. A woman of 29 who had chills and a temperature of 39.1° C., pulse 128, and dry skin, and was very restless and thirsty on the third day after delivery, was given 3 injections of 0.01 Gm. ($\frac{1}{10}$ grain) of mercuric benzoate in the course of three days, under which the temperature and pulse subsided to normal. Krohl (Berl. klin. Woch., Oct. 20, 1913).

Mercury dyestuffs exert some favorable influence on staphylococcic septicemia. One compound, benzurin, saved animals from infection to the extent of 70.8 per cent. Mercury can be detoxified considerably by combination with dyestuffs. Raiziss, Saverac and Moetsch (Jour. of Pharm. and Exp. Ther., Jan., 1926).

Nutrition.—Many years ago Liégeois was led to conclude that even in healthy men very small doses of mercury lead to an increase of weight. Schlesinger, in a series of experiments in sheep, rabbits, and dogs, also noted this fact. Having administered mercuric chloride for an entire year, he found that all the animals, especially the dogs, treated had gained in weight and that there had been a marked increase of red corpuscles, while none of the untreated control animals presented similar changes. There is much clinical testimony, moreover, to sustain the assertion that minute doses of mercury benefit nutrition. The fact that von Boeck found an increase—though slight—of nitrogen in the feces and urine under mercury tends to corroborate this.

Absorption and Elimination.—According to Conti and Zuccola, mercury, by whatever route introduced, is taken up by the leucocytes and transported thereby to various or-

gans, principally the liver, intestines, and kidneys. The liver appears to store it up, while the intestines and kidneys eliminate it. It is only inconstantly to be found in the glands, and is present there only when the system is oversaturated with it. It is always found by preference in the nuclei of the cells.

Ullmann, administering insoluble salts of mercury, found the metal deposited in the following organs, those containing the larger amounts being given first: kidneys, liver, spleen, intestinal canal (containing an increasing amount from above downward), heart, skeletal muscles, and in some cases lungs, and blood collected in the great vessels.

The elimination of mercury depends upon the manner in which it has been administered. Byasson and Betelli found mercury in the urine and saliva two hours after ingestion. After intravenous injection it may be detected in the urine within an hour, but after inunction may not appear for twenty-four hours. Riederer obtained, from the feces of a dog, 77 per cent. of the quantity administered during thirty days, and from its urine 1 per cent.

Mercury is likewise eliminated by the salivary glands, stomach, liver, and skin, and has also been found in the milk of nursing women, in their sucklings, and in semen. The experiments of Magençon and Bergeret tend to show that a single dose of mercury is completely eliminated in a relatively short time. It is known, however, that after the ordinary type of mercurial treatment in syphilis the metal may be found in the urine for months and at times years after the last dose taken.

Mercury found in the urine of dentists who had been working with amalgam fillings; one dentist had 3.4 mg. to the liter of urine. Blomquist (*Hygeia*, Apr., 1913).

After poisoning a rabbit with mercury, the writer found the metal in the blood and lymph; also in the walls of the intestine, in the state of insoluble sulphide. This is due to the action of hydrogen sulphide in the intestine on the metal. The granules of mercury may be carried by the leucocytes between the epithelial cells of the intestine. Other granules are found in the walls of the blood-vessels. If these granules are numerous enough to obstruct the circulation, they may cause necrosis and ulceration. The amount of mercury sulphide precipitated is not proportional to the amount of mercury introduced, but to the amount of hydrogen sulphide in the intestine. Almkvist (*Nord. Med. Arch.*, Nov. 6, 1903).

UNTOWARD EFFECTS AND POISONING.—Mercurial Salivation and Accompanying Phenomena.—

When there exists in the individual treated an unusual sensitiveness to mercury or the drug is given too long or in excessive quantities, symptoms appear that are quite pathognomonic. There is, at first, disagreeable metallic taste, the breath becomes fetid,—the fetor of dead tissue,—the gums are sensitive, and when the jaws are forcibly closed slight pain is experienced. At the same time the salivary flow becomes more free than usual. If the administration of the drug is not stopped as soon as these symptoms appear, the gums become spongy and bleed easily, the tongue swells, and the flow of saliva becomes very excessive,—ptyalism. If the gums be examined, a dark line will be found at their junction with the teeth. The parotid and maxillary

glands are usually enlarged and tender, and there may be slight fever, albuminuria, and oliguria. Frequently in rabbits, less often in man, glycosuria is evoked by prolonged use of mercury.

Persistence in the use of mercury after these manifestations is followed by local destructive changes. Ulceration of the mucous membrane, soon invading the deeper tissues; looseness and loss of the teeth, necrosis of the jaw bones, and copious hemorrhages occurring because of ulceration of the vascular coats follow in more or less rapid succession, and the patient dies of exhaustion. It is rare that such a result occurs nowadays. The cases of mercurial poisoning usually met are due, as a rule, to insufficient instructions to the patient, who continues to use the remedy without consulting his physician. Salivation is produced with particular ease in cases with nephritis; a single grain of calomel may induce it in such patients. A number of cases of gangrenous stomatitis, some fatal, following injections of gray oil have been reported.

Case of a syphilitic woman who had been given 2.75 c.c. (44 minims) of 50 per cent. gray oil during a period of one month, the first injection being 0.5 c.c. (8 minims). She had lost 11 teeth. Much of the right alveolar process was denuded. There was an excessive flow of saliva, which had continued six weeks. The patient had lost about 40 pounds in weight, and the skin seemed transparent and bluish.

The cavities in the jaw were washed with sodium bicarbonate solution and packed with iodoform gauze, the mouth syringed frequently with soda solution, and the dressings changed twice daily. The patient took potassium iodide, and tincture of iodine was painted on the gums.

The urine showed a heavy ring of albumin, some coarsely granular casts, pus, and epithelial cells. All bowel movements were watery and contained shreds of mucous membrane. The heart was found dilated, with very weak sounds, and *digitalis* ordered. The patient gradually grew weaker, and died after a slight exertion in rising in bed. T. E. Carmody (Denver Med. Times, Feb., 1913).

The severe dermatitis, edema of the skin and mucous membranes, and bloody diarrhea observed by the writers following use of mercury on the scalp, as a mouth wash, or subcutaneously, are held to represent anaphylactic manifestations. In several cases the use of the remedy had just previously been interrupted for a period, and in 2, phenomena of anaphylactic shock, such as leukopenia and fall of blood-pressure, were noted. Desensitization by repeated ingestion of small doses such as 0.01 Gm. ($\frac{1}{16}$ grain) of calomel proved feasible. The use of a small prophylactic dose before an injection is also suggested. Gougerot and Blamoutier (Bull. Soc. méd. des hôp. de Paris, June 8, 1922).

Good results claimed in the prevention of mercurial stomatitis by discarding the tooth-brush and having the mouth cleansed with cotton wrapped around the finger and by washing it out frequently. At night loose gauze is used to clean the floor of the mouth and between the teeth and cheeks. Gauze is left in the mouth over night to take up the mercury-laden saliva. Heermann (Münch. med. Woch., Apr. 28, 1922).

In some cases the skin is first to show the mercurial manifestations, an eruption resembling that of scarlatina being most frequently observed. Great suffering is sometimes entailed by a burning sensation of the skin, which may be markedly swollen and later exhibit abundant desquamation, at times extending even to the hairy scalp and mucous membranes.

Absence of fever and throat inflammation are features distinguishing the condition from scarlet fever. Where mercury has been applied externally, the eruption may start at the point of application and then extend elsewhere. The duration of mercurial eruptions is usually one to three weeks, at times longer.

Case of a healthy woman of 32 who gave a history of having suffered at her previous confinements from an eruption of the lower abdomen, inner surface of the thighs, and around the anus, which she attributed to the use of corrosive sublimate for cleansing the parts. Care was, therefore, taken to avoid mercurial preparations for sterilization purposes. After the child was born, however, and before the placenta had been removed, the midwife sterilized her hands in a solution of 1:1000 mercury oxycyanide, and then expressed the placenta. The same evening the patient complained of a smarting in the region of the umbilicus, and a patch of erythema was noticed corresponding in position to the place where the midwife's hands had rested when applied to the fundus uteri. Next day the affected skin was red and slightly raised, with minute vesicles scattered over it. The fluid was at first colorless, but gradually became turbid and yellow. Itching was present. The erythema faded gradually. Tissier and Corpechot (*Progrès méd.*; Hospital, Oct. 22, 1910).

Mercury may call forth almost as many cutaneous reactions as arsphenamin. It is well to bear this in mind when a patient receiving mixed treatment develops an eruption, for it may be due to either drug or to the combination. Eruptions may result either from external or internal use. They may be due to an idiosyncrasy or occur as part of a general intoxication resulting from the prolonged use or overdosage of mercury. C. S. Wright (*Arch. of Derm. and Syph.*, Oct., 1924).

A plaster containing mercury was found to sensitize the part to which it had been applied. Whenever an intravenous injection of mercury cyanide was given, an eruption appeared exclusively at the area where the plaster had been used.

Months later this area flared up when irritated by a compress of formalin, though less severely than it had after a mercurial injection. This peculiar allergic phenomenon was cured or desensitized by a dose of X-rays. S. Nicol (*C. r. Soc. de biol.*, Dec. 19, 1924).

A man, to destroy crab lice, vigorously rubbed in gray ointment 5 times in 60 hours. Symptoms suggestive of intussusception or dysentery followed. Hamburger (*Ned. Tijd. v. Gen.*, Jan. 30, 1926).

Anorexia, epigastric discomfort, nausea, and diarrhea, sometimes alternating with constipation, are other frequent manifestations of mercurial poisoning.

A middle-aged man with hyperchlorhydria took calomel when he was feeling unwell, in a very unusual dose—1 grain (0.065 Gm.) every half-hour for 11 doses. The red cells descended to 1,252,000 and the hemoglobin to 19 per cent.; at this point the tide turned, and the patient recovered. Fever, rapid pulse, a heart murmur, and general weakness, suggesting septic endocarditis, were noted. There was no marked salivation.

Another case was that of a woman who after a single douche of a solution of bichloride of mercury in the strength of 1:5000 developed typical symptoms of corrosive chloride poisoning. After all traces of hemorrhage from the mucous membranes had ceased, the red cells and hemoglobin continued to fall despite all treatment until they reached 1,200,000 red cells, hemoglobin 17 per cent., at which point the patient expired. W. G. Elmer (*Therap. Gaz.*, Sept., 1910).

Fatal case of poisoning from an injection of a 50 per cent. ointment

of mercury in hydrated wool-fat. It was ascertained afterward that the patient was being treated for chronic nephritis. Stress laid on the importance of bearing in mind, whenever mercury is used, especially in hypodermic form, the need of repeated examination of the urine. T. J. Harris (Amer. Jour. of Dermat., May, 1911).

Case of a man who, having been ordered to take pills of bichloride of mercury for two weeks after an operation for glaucoma, continued to take them for four months, the daily dose being $\frac{1}{8}$ grain (0.01 Gm.). Ulcerative colitis developed with diarrhea, and the patient succumbed in the fifth month to the results of perforation of an abscess in the rectum. There had not been any marked subjective disturbances at any time—no stomatitis—and all the organs appeared intact except the large intestine. Cobliner (Arch. f. Verdauungskrankh., Aug., 1911).

Case of unusual sensitiveness of the colon to mercury. The author, while treating a case of eczema, gave a course of salicylate of mercury injections. A 10 per cent. suspension in liquid petrolatum was used. On the morning after an injection of 15 minims (1 c.c.) into the buttocks, the patient suffered from severe tenesmus and bloody stools, with intense pain across the abdomen below the navel. About a week later a second injection was given with similar results. Montgomery (Jour. Amer. Med. Assoc., Mar. 23, 1912).

Besides the symptoms of mercury saturation which have been called "mercury gripe"—gastric distress and stomach or bowel disturbances which yield readily to an oil purge—the author has met with 4 cases in which mercury caused symptoms suggesting angina pectoris. In 1 case the pain was so intense as to cause syncope. The urine showed a little albumin, the pulse ran up, and the temperature also rose slightly. This pseudoangina pectoris was observed

twice in the course of treatment in 3 cases; it followed the fourth, sixth, or ninth injection in 3 cases, and the first in 1 case. The mercury can be continued without fear of further trouble after waiting two weeks. Albuminuria calls for reduction of the dose of mercury, but skin manifestations are generally due to special idiosyncrasy. Ragusin (Semana Medica, Sept. 5, 1912).

The author found in the literature since 1883 records of 108 fatalities from the use of mercury. In but 1 case had it been given by mouth (5 pills of 0.06 Gm.—1 grain—each). One fatality was credited to inhalation of mercury, 9 to mercurial oil, 10 to mercuric salicylate (in 1 case a single injection of 0.05 Gm.— $\frac{1}{2}$ grain—proved fatal), 7 to injection of the soluble preparations, 48 to injection of insoluble, 31 to gray oil, and 19 to inunctions. Stress laid on previous urine examination, and repeating once a week. Wolffenstein (Berl. klin. Woch., Oct. 13, 1913).

In an infant 18 months old, a 10 per cent. *mercurial salve* was applied for two weeks to patches of eczema back of the ears. Then the dermatitis rapidly became universal and severe nephritis developed with high fever, albuminuria, dyspnea and diarrhea. The latter was kept up with compound licorice powder, half a teaspoonful three times a day, and improvement gradually followed. Lomholt (Ugeskr. f. Laeger, May 3, 1917).

Treatment of Salivation.—The prophylaxis of "ptyalism" consists in having **carious teeth attended to** before mercurial treatment is begun, and in maintaining scrupulous **cleanliness of the mouth** during its entire course. A mouth-wash consisting of saturated **potassium chlorate** solution, with, perhaps, a little **tincture of myrrh** added, is recommended both for prophylactic and curative purposes. Where salivation definitely makes its appearance the **mercury**

should be discontinued or the dose greatly reduced.

Atropine may be given to arrest the elimination of the drug in the mouth, and an astringent mouth-wash containing **tannic acid** is also appropriate. Purging with **magnesium sulphate** may be of advantage.

Prophylactically, Freshwater advises the use after every meal of a small **tooth-brush of badger's hair**, together with employment of a mouth-wash of 5-volume **hydrogen peroxide** every hour or two.

In the stage of mercurial stomatitis in which there is complaint of tenderness of the palate behind the incisors, the writer covers the point of a fine bristle with cotton, saturates it with pure **chromic acid**, and applies this carefully around the necks of the teeth. In the more advanced cases with marked ulceration and acute pain, he directs that a syringe be used with **hydrogen peroxide** and warm water between the teeth to remove loose matter, then goes carefully around with cotton, using cotton pellets and tweezers, to remove as much as possible of the tartar, etc. After another wash with peroxide and water, the gum margins are swabbed with chromic acid on cotton and tweezers, followed at once with peroxide and water (equal parts), which prevents severe caustic effects. Considerable relief follows the 1st hour or 2 of discomfort. Used after every meal, the peroxide mouth wash is very beneficial. At the 2d examination, 2 days later, the **teeth** can be **scaled** without unusual pain. Chromic acid is again applied. A **milk diet** accelerates recovery. Foreman (Jour. Roy. Army Med. Corps, May, 1923).

CHRONIC MERCURIAL POISONING.—When mercury is inhaled in the form of a vapor, as by workers in thermometer, mirror, and hat factories, and in mercury mines, the nervous system is most apt to suffer, and paralysis is a frequent sequel.

The palsy may, after long exposure, come on either suddenly or slowly. Leyden, Spillmann, and others have recorded cases of pronounced multiple neuritis resulting from the therapeutic use of mercury. There is a species of general tremor and great unsteadiness in all movements, including those involved in locomotion, and the skin becomes dark yellow or brown. Mercurial "erethism," manifested in unusual irritability and timidity, with marked motor weakness and at times delirium, is a characteristic feature. Mental debility may appear, the precursor of an early demise. The manifestations often simulate chorea and paralysis agitans. The disease may assume various special forms, certain parts being more involved than others. In some cases wrist-drop is a feature; in others there may be a brachial or crural monoplegia, etc. Wasting of the muscles, however, does not occur, and the reaction of degeneration is absent. The special senses are often impaired (anosmia, deafness, amblyopia), and disorders of sensation are frequently observed. Neuralgia is a prominent feature. According to Gilbert, a blue line on the gums, very similar to that found in lead poisoning, may be present.

Description of the chronic and usually rather mild form of mercurial poisoning which develops in those manufacturing felt hats. The patient's mouth shows: Slight salivation; tongue large, flabby, and dove-colored or silvery; teeth blackened, especially near the crowns; there is usually some pyorrhea. These changes are most marked in tobacco users. The gum edge is often cyanosed. Many first complain of a tremor, rather fine, rapid, and of irregular amplitude. It is generally increased on voluntary movements, stops dur-

A large abscess formed on the left side under the bicuspid, and coincidentally there was an acute otitis media, with intense pain over the back of the head and neck. The eardrum ruptured and there was complete loss of hearing on the left side. The alveolar process on both sides necrosed and a large number of sequestra were removed. The patient finally recovered, but still suffers from anemia, weak heart, and nephritis. A number of the teeth dropped out or were removed by the patient. Herzstein and Boer (Jour. Amer. Med. Assoc., Mar. 23, 1912).

Case of a female aged 22 who swallowed 3 white bichloride tablets of 7.3 grains (0.5 Gm.) each. About ten minutes afterward the **stomach was emptied by tube, and repeatedly washed, with egg and milk**, for one-half hour. There were no signs of collapse. She was discharged on the twenty-fourth day as cured.

The treatment followed consisted of **hot packs, wet cuppings over kidneys, saline instillation per rectum, pilocarpine in ¼-grain (0.016 Gm.) doses, bismuth subnitrate**, and occasionally **tincture of opium, Vichy, and milk**. After kidney action was established **potassium citrate** was given in 10-grain (0.6 Gm.) doses, four times daily.

Interesting points in the case were: (1) Anuria for over five days, save for the passage of 10 drops in the ninetieth hour; (2) temporary presence of sugar in the urine for nine days; (3) bluish discoloration of the fingers, toes, urine, and vomitus, without the ingestion of anything containing methylene blue. J. M. Lobsenz (N. Y. Med. Jour., July 26, 1913).

According to Sollmann, the lethal dose of mercuric chloride is 12 grains (0.8 Gm.). Bunting points out that mercurous chloride (calomel) is very inconstant in its action as a poison. Six grains (0.4 Gm.) have proven fatal, while 1 ounce (30 Gm.) has

been taken with impunity. Rungberg records a case in which 3 injections of 1½ grains (0.1 Gm.) each, given within a month, proved fatal. These variations would seem to support the theory that calomel acts only by partial conversion into the bichloride, the extent of its poisonous action, therefore, depending upon varying factors such as the degree of acidity of the gastric juice. Recent observations, however, do not support this. Pouchet asserts that the bromides and chlorides are powerless to convert calomel into corrosive sublimate, such a change occurring only upon contact of calomel with the alkaline iodides.

The writer found in the literature 14 fatalities from the therapeutic use of calomel, death occurring in from three to forty-two days after a total dose of from 0.3 to 2.6 Gm. (5 to 40 grains) in 7 cases, and in the others after a total dose of from 2.4 to 4.6 Gm. (37 to 70 grains). The production of bile is diminished after calomel, and the drug has an irritating action on the kidneys. Chodounskey (Wiener klin. Woch., Apr. 7, 1910).

Case of a man 85 years of age who swallowed 8¾ grains (0.55 Gm.) of bichloride of mercury. At once recognizing his error, he drank a tumblerful of **barley water**. Seen half an hour later, he was given **white of egg**, and brought up blue-stained mucus from the indigo in the bichloride tablet. The **stomach-tube** was then passed and the **stomach washed out** with large quantities of **albumin water and milk and water**. There was an urgent desire for the bowels to move, but little more than mucus was passed. The patient collapsed, was cold and pallid, and the pulse was almost imperceptible. **Strychnine** was given hypodermically and **milk and brandy** by the mouth. The next morning he was somewhat better. For several

days the bowels continued to be very irritable, but after a slow convalescence he quite recovered from the effects of the poison. Fuller (*Brit. Med. Jour.*, Jan. 18, 1913).

In a fatal case, that of a woman who had taken upon an empty stomach a large teaspoonful of corrosive sublimate in powder form, Durante found the following pathological changes: Subpericardial ecchymoses; enlarged liver, with subcapsular ecchymoses; pale, swollen kidneys, with small ecchymoses in the pelves; esophagus reddened at its upper part, normal below; stomach showing a softened mucosa, with numerous ecchymotic patches and large, grayish ulcerations, most marked near the fundus; intestinal mucosa showing limited areas of deep reddening, with ulcerations, the changes in the large intestine being less than those in the ileum; brain showing injection of the vascular meninges.

In an illustrative case reported by R. L. Dixon the renal tissue showed a large amount of lime salt deposit, a consequence of decalcification of the bones, as noted especially in the sternum; the case also showed a marked congestion of the hemolymph-nodes in the retroperitoneal tissue.

Local applications of various preparations of mercury are no less toxic than when the drug is taken by the mouth. Sackur reports the case of a girl aged 20 who sprained her wrist. A few days later lymphangitis apparently supervened, for which mercurial ointment was applied and rubbed into some cracks on the hand. An hour after the inunction the patient felt ill, fainted, and vomited. The same evening there was much

swelling of the hand and of the arm on its dorsal aspect. An incision was at once made. On the succeeding days there occurred vomiting, tenesmus, albuminuria, anuria, blood-stained stools, gangrenous gingivitis and glossitis, prostration, paralysis of the extremities, and death.

The recommendation of preparations of mercury for vaginal douching is attended with danger, owing to the large quantity of fluid injected. Rectal injections are still more dangerous, owing to the rapidity with which fluids are absorbed.

Report of 3 cases in which patients had been instructed to "use" bichloride tablets. Each of them inserted 1 tablet in the vagina. Although medical assistance was obtained within twenty to thirty-five minutes the patients died, respectively, four, fourteen, and seven days later. It would appear that a fatal amount can be absorbed from the vagina within twenty minutes. The patients were unable to remove the tablets themselves because of severe spasm and pain. C. B. Schildecker (*Amer. Jour. of Obstet.*, Mar., 1911).

Case of poisoning from vaginal douches of mercuric chloride solution, 1:1000 to 1:2000 strong, used to prevent conception. Beekman (*Jour. Amer. Med. Assoc.*, Feb. 14, 1914).

Case of woman who exhibited a violent reaction to injection into the nose, to act on the lacrimal sac, of 1 c.c. of a 1 per 10,000 solution of mercuric chloride containing a little adrenalin. Possibly her recent conception may have increased the susceptibility. Cjessing (*Norsk. Mag. f. Laegevid.*, Mar., 1918).

Sajous has pointed out that mercury is a powerful adrenal stimulant. The addition of adrenalin, and the stimulation of the adrenals resulting from the conception plus the mercury, account for the toxic phenomena. EDITORS.

Treatment of Acute Mercurial Poisoning.—In the classic treatment of these cases, the **whites** of several **eggs** are at once administered, in order to form non-corrosive albuminates with the mercury. Complete precipitation of the mercury is not to be relied on, however, and the **stomach** should be **evacuated** soon after and **washed out**, using a **stomach-tube**. In the absence of the latter, **emesis** may be resorted to. As soon as the stomach has been well evacuated more white of egg should be administered and left *in situ*. If no eggs can be had **milk** or **wheat flour** may be used, the latter with a little water. **Finely chopped beef** might likewise be used. Non-irritant oils and other **demulcents** should be administered. **Opium** may be required to relieve pain and tenesmus. Nephritis and colitis should be treated by the usual measures. Where the oral cavity is foul, a solution of **hydrogen dioxide** is serviceable.

In the colic occurring during therapeutic use of mercury, the writer recommends, in particular, **adrenalin**, 20 drops of the 1:1000 solution in a little water 3 times a day; also **rest in bed**, a **daily full bath** at body temperature for $\frac{1}{2}$ hour, and **plenty of food**, in order that the contained proteins shall combine with the mercury. Upon resumption of mercury, smaller doses should be used, with a week between injections, and giving **calcium salts** and 40 drops of adrenalin daily. Milian (Paris méd., Dec. 11, 1920).

The Lambert and Patterson treatment, consisting of **alkalies**, **gastric lavage**, **colonic irrigation**, and **daily hot packs**, has greatly improved the results in these cases. Apparently, results nearly as good are obtainable merely by the lavage, free introduction of **fluids** and the **alkalies**.

In bichloride poisoning the writers **wash out the stomach** twice daily and also give 2 **colonic irrigations** daily. A liquid diet of 8 ounces of **milk** every 2 hours is given to be alternated every 2 hours with 8 ounces of the following mixture: **Potassium bitartrate**, 1 dram (4 Gm.); **sugar**, 1 dram; **lactose**, $\frac{1}{2}$ ounce (15 Gm.); **lemon juice**, 1 ounce (30 c.c.); **boiled water**, 16 ounces (500 c.c.). A solution containing 1 ounce (30 Gm.) of **potassium acetate** to the pint (500 Gm.) of water is also given continuously by rectum. The patient receives a **daily hot pack**. Among 16 cases thus treated there were but two deaths. Lambert and Patterson (Arch. of Internal Med., Nov., 1915).

Case with anuria in which an intravenous injection of **hypertonic dextrose solution**, 60 Gm. (2 ounces) in 200 c.c. ($6\frac{1}{2}$ ounces) of distilled water, caused striking improvement. Milian and Mougenc de Saint Avid (Paris méd., Sept. 8, 1917).

Hypodermoclysis or **rectal drip** and **hypertonic dextrose solution** intravenously, advocated. Achard (Paris méd., July 8, 1922).

Following treatment used in 135 cases, with only 8 deaths, or 6 per cent.: The **stomach** is at once **washed** through a tube with 2 quarts (liters) of saturated **sodium bicarbonate** solution, continued until the washings return clear. Before the tube is removed, 6 ounces (180 c.c.) of saturated **magnesium sulphate** solution are introduced and allowed to remain. A **soap-suds enema** is then given. As soon after the preliminary treatment as possible, an intravenous injection of **Fischer's solution** is given. (This consists of crystallized **sodium carbonate**, 10 Gm.; **sodium chloride**, 15 Gm., in distilled water, 1000 c.c.) If this is not available, 4 per cent. sodium bicarbonate solution may be used. In patients free of circulatory abnormality, 1 to 1.5 liters of this solution are easily tolerated. As much as 1800 c.c. has been given. The alkaline therapy is continued by mouth, using a solution of **potassium bitartrate**, 1

dram (4 Gm.); **sodium citrate**, 30 grains (2 Gm.), in a glass of water, orangeade or lemonade. The patient receives 8 ounces (240 c.c.) of this drink 6 to 8 times a day. The writer endeavors to make the urine alkaline to methyl red and keep it so. Large amounts of urine are thus usually voided and most patients show a normal urine on the 10th to the 14th day. Where over 7 grains of bichloride have been taken and there is marked urinary disturbance, a second, and at times a third, intravenous injection is given. Of 15 cases with complete suppression, 8 recovered. A liberal diet, including meat, is allowed after the diarrhea ceases. H. B. Weiss (*Arch. of Int. Med.*, Feb., 1924).

Renal decapsulation has been attempted in a few cases with anuria. Fatal uremia was forestalled, but the patients eventually succumbed to the other pathological conditions.

Sodium thiosulphate by mouth has been recommended by Salvatani; **calcium sulphide** by mouth and intravenously by Wilms, and **magnesium oxide**, 30 to 60 grains (2 to 4 Gm.) every 3 hours with plenty of water, by Schisler.

In a study of 141 cases of mercury poisoning, **magnesium oxide** and **sodium bicarbonate** proved best, yielding 92 per cent. of cures. The magnesium oxide is given in doses of 32 to 60 grains (2.1 to 4 Gm.) every 3 or 4 hours. This method has been used in conjunction with **gastric lavage**, **milk** and **eggs**, and the administration of 70 to 100 c.c. (2½ to 3½ ounces) of a saturated solution of **magnesium sulphate** as emergency treatment, followed by stimulation or sedatives as indicated. Brashear (*Med. Council*, Mar., 1920).

Intravenous injections of sterile solutions of C. P. **sodium thiosulphate** recommended. Three to 4 injections of 0.45 to 0.6 Gm. (7 to 10 grains), given intravenously in 5 c.c. (80 minims) of water on alternate days, proved

sufficient in mild cases to clear up the fetor and salivation, and permitted early dental treatment to insure against recurrence. There were good results in 3 cases of mercurial stomatitis, 1 with an eruption. H. C. Semon (*Brit. Med. Jour.*, Apr. 12, 1924).

The writers were able to save rabbits from a lethal dose of bichloride by giving sodium thiosulphate, 1 Gm. per kilo. of body weight, after the mercury. E. Hess and Massaro (*Jour. of Urol.*, Nov., 1925).

THERAPEUTICS.—Metallic mercury is mainly employed as a cathartic in the form of blue pill. As such it is deemed valuable when **hepatic torpor** appears to exist, though it sometimes proves irritating to the intestinal tract. Nine grains, or three 3-grain (0.2 Gm.) pills, usually give rise to little, if any, griping. If this symptom is feared, however, a little opium may be added. A saline purgative is given the next day.

Mercury with chalk, or gray powder, acts more mildly than blue mass and is, therefore, considerably used in the treatment of children suffering from **hepatic atony** and the **intestinal conditions** associated therewith. The antacid power of the chalk adds to its value in the treatment of **infantile diarrhea** with watery, colorless stools. It is also used in **infantile syphilis** with success, especially in syphilitic marasmus.

Mercurial ointment, besides its well-known value in the treatment of **syphilis** (*q.v.*), is also employed as an antiphlogistic and resolvent in **joint inflammations**. It is especially valuable when **effusions** and **ankylosis** are feared as a result of the local changes.

It is also considered of value by some to check serous effusions in **pleurisy**, **pericarditis**, and **peritonitis**,

as well as to promote healing in these conditions. The same may be said of **orchitis** and **epididymitis**, **glanders**, and other surgical mycoses.

Mercurial ointment has also been considerably used in the treatment of **pediculi** or other parasites of the hairy regions of the body; but as Leidy showed, any fixed or volatile oil or even a bland ointment will act as effectually. Hence mercurial ointment should only be employed after trying the less dangerous preparations. If it is used, care should be taken to avoid salivation.

Mercurial plaster may be used in the same disorders as the ointment and with the same objects in view. It is especially valuable in the treatment of **splenic enlargements** of **malarial** origin. It is also used to prevent pitting in **small-pox**.

Oxides of Mercury.—The yellow oxide of mercury is too irritating for internal administration, and is mainly employed to prepare the corresponding 1 per cent. ointment. The 10 per cent. ointment formerly official, too strong for ophthalmic use, was generally reduced by the addition of lanolin, lard, etc. According to T. E. Mitchell, the following method of preparing the ointment of yellow oxide is preferable to that officially prescribed, the mass produced being more thoroughly homogeneous:—

℞ *Olei ricini* gtt. iv (0.24 Gm.).
Hydrargyri oxidi
flavi gr. iij (0.2 Gm.).
 Misce et adde:—
Petrolati ʒij-iv (8-16 Gm.).

The red oxide of mercury is employed to prepare the corresponding ointment, but the latter is advantageously replaced by the ointment of the yellow oxide, owing to the

finer grain of the powder obtained with the latter.

Black wash and yellow wash, considerably used as local stimulants, depend for their virtues upon the black and yellow oxides formed.

The yellow oxide of mercury enjoys the confidence of ophthalmologists in the treatment of **blepharitis** and **conjunctivitis**. In the acute form of the latter disorder an ointment containing 3 to 4 grains (0.2 to 0.25 Gm.) of the yellow oxide to the ounce (30 Gm.) is sufficiently strong, while disorders of the lids usually require a preparation of four times that strength. The ointment should not, however, be allowed to come into contact with the conjunctiva. **Corneal opacities** and **ulcers** are also favorably influenced by the continued application of an ointment of yellow oxide of mercury.

Among affections of the skin the yellow oxide has been used with advantage in **eczema** and **acne**. **Erythematous pruritus** of the **anus** is quickly arrested by its use.

The red oxide is mainly used to stimulate **obstinate ulcerative processes**, such as those occurring in venereal disorders. It is also employed in **parasitic diseases of the skin**. Morain recommends a 2:15 ointment of red oxide in petrolatum in **anal pruritus**, while Elliott has found the following combination very useful in **acne** where much pustulation exists:—

℞ *Ung. hydrargyri oxidi*
rubri ʒiij (12 Gm.).
Ung. sulphuris ʒvj (24 Gm.).
Ung. zinci oxidi, q. s. ad ʒij (60 Gm.).
 M.

Varicose ulcers of the legs were successfully treated by Langes with

an ointment of 1 part of red oxide of mercury to 18 parts of petrolatum.

Black and yellow wash are also employed to stimulate **chancres** and **syphilitic ulcers**, the yellow wash being far more potent than the black. The latter has been used in **eczema**.

The oleate of mercury is sometimes substituted in syphilis for the much less cleanly agent, blue ointment. It should be rubbed into the tissues in somewhat smaller quantities, and less rapidly. It is also employed in **parasitic skin disorders**, having replaced gray ointment in many of these, especially **tinea tonsurans**, **pediculosis**, and **sycosis**.

Ammoniated Mercury.—The ointment of ammoniated mercury (white precipitate) is the most irritating of the official ointments of mercurial compounds, and is employed in such affections as **chronic eczema** and **psoriasis**. It is also used in **parasitic skin diseases**, and occasionally as an application to **syphilitic ulcers**.

Nitrates of Mercury.—The solution of acid nitrate of mercury is a very active caustic, instantly penetrating the superficial tissues and especially **phagedenic ulcerations**. When, therefore, it is to be applied, the spot to be touched should be surrounded by a protective coating of petrolatum, and a glass rod should be used for the application to limit precisely the amount employed. Any surplus should be washed off or removed with blotting paper. It has sometimes been used for the destruction of **syphilitic sores**, **benign** and **malignant neoplasms**, **lupus**, **condylomata**, **noma**, **nevi**, **warts**, etc. Shield reported a case of complete cure in **lupus vulgaris** from 6 applications of pure nitrate of mercury under cocaine local anesthesia.

Nine cases of **superficial new growths** treated by acid nitrate of mercury as recommended by Sherwell. The procedure consists in local anesthesia by cocaine; complete removal of the growth with curettes or scalpel; hemostasis by cautery if necessary, and, finally, application of the nitrate for fifteen to twenty minutes, followed by sodium bicarbonate to neutralize the excess. The resulting wound is kept clean and dry, the edema and swelling usually requiring no special treatment. The immediate and permanent results, both in benign and malignant growths, are excellent. H. H. Hazen (Wash. Med. Annals, Nov., 1912).

The ointment of nitrate of mercury, or citrine ointment, has been not infrequently employed for deep-seated inflammations limited to restricted areas, when the superficial tissues are intact. It was thus successfully used to abort **boils** and **felons** by Kenner, who, in treating a felon, covered the entire finger with a coating of the ointment about $\frac{1}{8}$ inch thick, and then wrapped over it a piece of thick adhesive plaster. This dressing was allowed to remain twenty-four hours, after which no further treatment proved necessary.

In **tinea circinata** the ointment of mercury nitrate has been found to be effective. When the ointment is to be used in **ulcerative processes**, for which it is employed as an active stimulant, it should be diluted one-half. In this strength it is especially useful in **chronic disorders of the scalp**, and is also occasionally used in **chronic eczema**, **psoriasis**, and other cutaneous disorders of the body, though only when these are localized. Its application over large surfaces is dangerous.

Iodides of Mercury.—The red iodide, or biniodide, of mercury is

used principally in the treatment of **syphilis** (*q.v.*), but it has been found useful in various other disorders, as an antiseptic in surgery, and in infectious diseases.

Illingworth used a 1:2000 solution of mercury biniodide in sodium iodide solution for the dressing of all **amputation flaps** and **recent wounds**, and asserted that union is secured more firmly and rapidly thereby than with phenol dressings. He found it non-irritant.

The same author used the biniodide both internally and locally in **scarlet fever**, with asserted good results both in causing the condition to abate and in preventing its transmission to others. The throat was painted or sprayed every four hours with a 1:2000 to 1:500 solution of the drug.

Hypodermic injections of biniodide of mercury are very effective in **hereditary syphilis**. Children tolerate large doses of strong solutions of the drug, and the writer recommends as an ordinary dose 0.06 Gm. (1 grain) at intervals of five to eight days, according to the severity of the specific manifestations. A perfect solution of the mercurial is obtained by adding a small quantity of potassium iodide, and for this purpose a few drops of the following solution is recommended: Potassium iodide, 1 Gm. (15 grains); distilled water, 4 c.c. (1 fluidram). Intramuscular injections are less painful than subcutaneous. Breton (*Revue mens. des mal. de l'enfance*, Dec., 1903).

Favorable effects observed in **syphilis** from intramuscular injections of mercury biniodide, $\frac{1}{4}$ or $\frac{1}{2}$ grain (0.016 or 0.021 Gm.). Cole, Driver and Hutton (*Jour. Amer. Med. Assoc.*, Nov. 25, 1922).

Biniodide of mercury precipitating tyrotoxin in liquids, it has been recommended as an antidote in **ptomaine poisoning**.

The green or yellow iodide is mainly employed in **syphilis** (*q.v.*).

The solution of arsenic and mercuric iodides (Donovan's solution) is much esteemed in the treatment of chronic disorders of the skin: **leprosy**, **lupus**, etc. It is also advantageous in **chronic gout** and in **rheumatism** as a general alterative and tonic.

Chlorides of Mercury.—*Mercurous chloride*, or *calomel*, is still considerably employed as a **purgative**, though slow in action and occasionally unreliable. The opportunity for retention under such circumstances renders mercurial absorption possible when a large dose is given, and it is always prudent to administer a saline the next morning, or to give another purgative at the same time—a poor recommendation for the primary drug. The compound cathartic pill is based upon this principle. Recent labors have severely shaken the general belief that calomel increases the flow of bile, and tend to confirm the view that as true purgatives there are many agents, *e.g.*, podophyllin, that are preferable to calomel. The latter is advantageous, however, over most other purgatives in having decided antiseptic properties, without inhibiting the digestive ferments. Its germicidal action may render it useful, moreover, in the presence of systemic infectious processes. In **diphtheria**, for instance, it is useful, and will sometimes check the disease when administered,—but this can hardly be credited to its merits as a purgative. According to the experiments conducted by Boyon and Dufour on dogs with bile fistulas, calomel actually exerts a decided inhibitory effect on the secretion of bile.

Sollmann explains the action of calomel in the intestines as the result of its being attacked, especially in the ileum, by the alkaline pancreatic and intestinal juices. These dissociate it into mercury and yellow mercuric oxide; the latter, according to Schaefer, dissolves slowly and incompletely in the intestinal fluid. Mercuric chloride cannot exist as such in the alkaline intestine. The dissolution of calomel in the intestine is slow, so that but little of the drug has actually become soluble when purgation begins.

Thus it is conceivable why purgative effects are obtainable from calomel with greater certainty and without danger of ptyalism when very small doses, $\frac{1}{10}$ to $\frac{1}{2}$ grain (0.006 to 0.03 Gm.), are administered every half-hour until 1 to 3 grains (0.06 to 0.18 Gm.) have been taken. Most or all of the mercury thus ingested becomes operative as a cathartic in the intestinal tract, and there is no surplus to awaken toxic symptoms later on.

Given in one large dose, calomel produces a cathartic effect with little constitutional disturbance. One-grain (0.06 Gm.) doses given at regular intervals of an hour for eight hours produce catharsis, plus some extra intestinal irritation, and plus a general constitutional influence. When the drug is given in doses of $\frac{1}{10}$ grain (0.006 Gm.) two or three times a day, a general glandular stimulation is induced, without special intestinal disturbance. H. B. Hemenway (Jour. Amer. Med. Assoc., Mar. 19, 1910).

Better results are obtained when calomel is allowed to complete a purgative action itself than where another purgative is given. There is less liability of secondary stasis immediately following such purgation, and the bowel discharges remain normal for some time there-

after. G. L. Servoss (Oklahoma Med. News-Jour., Sept., 1910).

Large doses of calomel have been recommended by some in the early stages of **acute febrile disease, pleurisy, pneumonia, yellow fever**, and even in such affections as **cholera**. It seems possible, from relatively recent experimentation, that calomel in moderate doses may have the power to activate the processes of immunity.

In **jaundice**, or "**biliousness**" due to **exposure to cold**, calomel is also employed with asserted benefit.

In children very small doses of calomel are of great value when general **inertia** is **associated with a heavy breath and (usually) ill-smelling stools**. Four doses of $\frac{1}{25}$ grain (0.0025 Gm.) each every half-hour, repeated in four or five days if needed, sometimes change the entire aspect of the child. The drug is best administered thoroughly mixed with a little sugar, the powder being merely placed on the tongue. The tonic action of the remedy plays an important rôle here, provided only minute doses are given.

In **infantile diarrhea** this treatment is decidedly valuable; $\frac{1}{20}$ grain (0.003 Gm.) of the drug should be administered every three hours.

As an **anthelmintic** calomel may also be used with advantage.

All the mercurial preparations possess **diuretic** properties, but these are especially marked when calomel is employed. The increase of urine may range from a few ounces to as much as 370 ounces (Jendrassik). When calomel is administered in moderate doses, repeated every three or four hours, the diuretic action appears early in some cases and only after four or five days in others. **Ac-**

cording to Lipari, tolerance for calomel is greatest where the diuretic action is most rapidly produced, while it is least where the diuresis is retarded. The main untoward feature in its use is the marked tendency to cause ptyalism and other manifestations of mercurial intoxication. Hence the patients should be carefully watched. Calomel is especially efficacious in **edema of cardiac origin**. Six doses of $1\frac{1}{2}$ grains (0.1 Gm.) each may be given during the day, one every three hours. After the first few doses have been given, as a rule, an increase in diuresis is established, and on the second or third day copious evacuations of the bowels take place. There is marked improvement in all the symptoms, cardiac and other. Even after the calomel has been discontinued these good results persist for from twenty-four to forty-eight hours.

In order to prevent excessive salivation, or to relieve it when already produced, the following mouth-wash may be used:—

R Potassii chloratis ... ʒiiss (10 Gm.).
Acidi tannici gr. iv (0.25 Gm.).
Aqua destillata fʒx (300 c.c.).

M.

The calomel does good by relieving the congestion of the liver and the renal circulation, thus indirectly reducing the resistance to the heart. At the same time an absolute milk diet should be ordered. Of 107 cases of grave **cardiac disease** with distressing symptoms of failure of the heart treated in this manner by Moraldescu there were 14 deaths: 2 died of pneumonia after the heart symptoms had been relieved; 3 died before the treatment had sufficient opportunity to be tried, and the remaining 9 were of ad-

vanced years and the disease also was far advanced.

Mercury is especially of value when there is no concomitant renal or hepatic disorder, and is harmful, according to Huchard, when the urine contains albumin. Pathological changes in the kidneys, indeed, prevent or abridge its action.

According to Landau, calomel is appropriate in severe **dropsy** not only when due to **valvular disease**, but also when due to cardiac failure from **fatty degeneration, atheroma, and myocarditis**. In **fatty heart** he considers it in some ways a specific, as it not only causes profuse diuresis, but causes the absorption of fat. He advises that it be given for six to eight days in about 1-grain (0.06 Gm.) doses five times in twenty-four hours, at intervals of three to four hours. Profuse diuresis sets in, as a rule, on the fifth day. The calomel should be still continued until the dropsy quite disappears. On the sixth or seventh day, when diuresis is fully established, infusion of digitalis may be prescribed with additional benefit. If the dropsy has not disappeared after the first course, the treatment may be repeated after an interval of a week. Mild stomatitis, gingivitis, colic, bloody stools, hoarseness, etc., need not interrupt the calomel treatment. Should, however, diarrhea be severe, the dose may be reduced to 3 or 4 powders a day (Landau).

Calomel has also been used as a **diuretic in renal and hepatic disorders**, but the results are less constantly favorable. Its behavior in the treatment of cardiac disorders would tend to demonstrate that renal lesions inhibit calomel diuresis; hence the propriety of prescribing calomel in these

cases seems doubtful. Yet in a certain proportion of instances of **nephritis** calomel undoubtedly proves superior in action to all other diuretics.

In **hepatic cirrhosis** with **ascites** calomel can be given in moderate doses with safety. Zakharine has recommended its use both in **cholelithiasis**, **catarrhal jaundice**, and **hypertrophic cirrhosis of the liver**—where the usual measures have failed—in doses of 1 grain (0.06 Gm.) every hour for five consecutive hours, after which, in cirrhosis, it is further administered every two hours until pain has disappeared.

In **lupus**, especially in an old, ulcerated, turgescient form, with deep infiltration, Asselbergs found injections of $\frac{3}{4}$ grain (0.05 Gm.) of calomel (into the buttocks) of decided, though not always lasting, value.

Calomel has been used **locally** as a stimulant in chronic inflammatory and ulcerative processes of the skin and mucous membranes, but its possible toxic effects impose caution in this direction. In **syphilitic ulcers** it may be used as a dusting powder. When it is used in **phlyctenular conjunctivitis**, potassium iodide should not be given simultaneously, as a highly irritating compound would otherwise be formed.

Mercuric chloride, or *corrosive sublimate*, aside from its uses as an antiseptic (see WOUNDS), and in **syphilis** (see SYPHILIS), is possessed of useful applications very similar to those of calomel, doses commensurate with its greater strength being, of course, employed. Here, again, the activity of mercury as a tonic becomes manifest, provided very small doses are adhered to.

In the **summer diarrhea** of children

and adults very small doses of mercuric chloride are especially effective— $\frac{1}{100}$ grain (0.0006 Gm.), repeated every hour or two.

In **dysentery** enemata of mercury bichloride were successfully employed by Lemoine and others in cases where ipecacuanha had failed, and where the patients complained from the beginning of nausea and vomiting. A 1:5000 or 1:6000 solution of the bichloride was used, and enemata of 6 fluidounces (200 c.c.) each were given once to three times daily.

The drug has also been recommended in the treatment of **diphtheria**, $\frac{1}{100}$ grain (0.0006 Gm.) being given every three hours; in no sense does it replace antitoxin, but where benefit from the latter seems delayed, addition of small doses of mercury has frequently been followed by gratifying improvement.

Subcutaneous injections of the bichloride have been recommended in a variety of affections. Thus, Jullien lauds treatment of this kind in **gonorrheal rheumatism**. Consalvi and Smith have reported good results in **cerebrospinal meningitis** from injections of $\frac{1}{15}$ to $\frac{1}{4}$ grain (0.004 to 0.015 Gm.). Smith gave the larger dose at first, and then $\frac{1}{15}$ grain every hour until gastrointestinal irritation appeared. In **pernicious anemia** De Francesco and Patera also claim benefit from repeated injections of the drug.

The author highly recommends the use of bichloride of mercury in infectious and contagious diseases. For many years he has used it with good results in **scarlet fever**, **measles**, **pertussis**, **la grippe**, **pneumonia**, and **typhoid fever**, provided they came under care early, before complications or profound toxemia had developed, without a complication or death. He has also treated **intestinal diseases**

in children with bichloride, without a single death in cases that came early. The dose is $\frac{1}{16}$ to $\frac{1}{8}$ grain (0.004 to 0.008 Gm.) every two or three hours for an adult; for children, in proportion, except in severe syphilis. He administers $\frac{1}{16}$ to $\frac{1}{8}$ grain (0.004 to 0.008 Gm.) hypodermically once a day for four days, and then twice a week for three weeks, and also gives during the hypodermic medication $\frac{1}{16}$ to $\frac{1}{8}$ grain by mouth, five or six times daily, continuing the drug for several months, or longer, if necessary. As soon as the gums swell and the teeth become slightly tender, one should stop the drug for a few days, later resuming it. H. E. Jones (Va. Med. Semi-Monthly, Jan. 22, 1909).

Intravenous use of bichloride of mercury recommended in the not infrequent cases of **septicemia** in which the micro-organism responsible remains obscure.

Even where the infection was so severe that the patient's condition seemed hopeless, the writer obtained almost miraculous results. He employed the following formula:—

R *Hydrargyri chloridi corrosivi* . gr. $\frac{1}{16}$ (0.01 Gm.).
Sodii chloridi . . gr. $\frac{1}{4}$ (0.075 Gm.).
Aquæ sterilisatæ . f3iiss (10 c.c.).

M.

This is slowly injected into a vein. The same dose may be injected 3 times in 24 hours. Baccelli (Policlinico, No. 13, 1911).

The writer administered $\frac{1}{32}$ grain (0.002 Gm.) of mercury bichloride 3 times a day to over 200 cases of non-syphilitic nursing mothers whose infants had vomiting, diarrhea, colic, lack of gain in weight, constipation, or skin manifestations (eczema or urticaria). Between 30 and 40 per cent. were benefited. The weight increased rapidly in many cases where it had been stationary. It was rarely necessary to continue the drug for more than four weeks, although in a few cases it was continued for months. Haas (Arch. of Ped., July, 1912).

Many non-specific curative effects of mercury occur in non-syphilitic diseases, *e.g.*, the good results in **sympathetic ophthalmia**, in various forms of **uveitis**, including the traumatic form, and in **optic neuritis**, especially toxic retrobulbar neuritis. Non-syphilitic nervous diseases sometimes favorably influenced include **tumors of the brain and spinal cord** and local and serous **meningitis**. There is also frequently a curative action in **tuberculosis of mucous membranes**. There can be no question of an activation of protoplasm such as is induced in non-specific protein therapy. An initiation of chemical or physico-chemical action by the mercury seems to be concerned in the effects. Buschke and Sklarz (Deut. med. Woch., Nov. 17, 1922).

The external uses of mercury bichloride are very numerous. In the treatment of **furunculosis** or **boils** it is extremely valuable, and often succeeds in arresting them when used early. Compresses of a 1:500 solution applied over the spot—or, when the furuncle shows its first signs on an extremity, baths of this strength—are efficient.

In **onychia maligna**, **glanders**, and **anthrax** these applications are also of value. The effect is enhanced by using warm solutions. In **smallpox** the salt is distinctly effective in the prevention of pitting. Talamon for this purpose proceeds as follows:

On the first or second day of the eruption, the face is washed with soap and water, rinsed with borated water, and wiped dry with absorbent cotton. After the third day the washing is unnecessary. The eyes are protected with borated wadding, and a solution of mercury bichloride applied with an atomizer. The spray is applied chiefly to incipient pustules. Fifteen minutes after this operation of atomizing, which should not last more than a minute, the face is rubbed with a pledget of wadding dipped in a glycerin solution of sublimate of the strength of $\frac{1}{2}$ dram (2 Gm.) to the

fluidounce (30 c.c.). The procedure is repeated three or four times a day in the first three days, and then twice until the sixth or seventh day, when the spray is suspended and the glycerin painting continued until the scabs begin to drop off. The results are highly successful except in cases of confluent smallpox. The spray solution is made up as follows:—

R *Corrosive sublimate*,
Citric acid ... of each gr. xv (1 Gm.).
Alcohol ℥lxxv (5 c.c.).
Ether q.s. ad f̄xiiss (375 c.c.).

M.

Solutions of mercury bichloride in distilled water are far more permanent than those in tap water, decomposition at once setting in in the latter and being kept up through the influence of air and light. Sodium or ammonium chloride hastens the solution of the mercury salt in water, but their presence distinctly impairs the antiseptic power of the bichloride, the dissociation of which into ions, as well as the precipitation of proteins by the bichloride, is hindered.

Cyanides of Mercury.—The oxy-cyanide of mercury has been highly lauded as an antiseptic in surgery. It is well tolerated by the tissues, and is considered especially applicable to suppurating surfaces or mucous membranes, *e.g.*, the conjunctiva, to render them aseptic.

As a disinfectant for metallic instruments, oxycyanide of mercury is advantageous in that it does not in any way affect the latter, not even the edge of cutting instruments. A 3 per cent. solution corresponds in power to a 2 per cent. solution of corrosive sublimate, but a 1:10,000 solution has been found efficacious for external uses. Monod and Malgaigne found it to possess all the qualities of the bichloride. The drug being exceedingly toxic, they never use

large quantities at a time and avoid using it for washing out cavities.

Chibret administered injections of a 1 per cent. solution of the oxy-cyanide in over 1000 cases of **sypilis**, without untoward effects in any instance. Galezowski recommends the following formula for routine use in the treatment of **choroidal atrophy** in cases of **myopia** and of **disseminated choroiditis in gouty persons**:—

R *Cocaine hydro-*
chloride gr. iv (0.25 Gm.).
Mercury cyanide ... gr. i. ss (0.3 Gm.).
Cherry-laurel water. f̄vj (25 c.c.).
Distilled water f̄vij (250 c.c.).

M.

The same solution may be used for subconjunctival injection in certain cases of severe **exudative** and **plastic choroiditis**.

The cyanide of mercury is highly recommended in 1:2000 solution as an antiseptic for use by oculists, and is non-irritating.

It has been recommended as a safe agent for hypodermic use. According to Harrington's experiments, mercury cyanide is not to be relied on as a general surgical disinfectant.

Subconjunctival injections of cyanide of mercury employed in numerous cases of **trachomatous keratitis**, **acute indolent ulcers**, **ulcer hypopyon**, recent **corneal opacities**, **parenchymatous keratitis**, and **episcleritis** and **scleritis**. Ten to 20 minims (0.6 to 1.25 c.c.) of a 1:4000 solution in sterile water were injected. Within an hour or so all discomfort disappeared. The results were very satisfactory. **Blepharospasm** and **lachrymation** were promptly relieved. Pain in scleritis and ulcers ceased. Recent corneal opacities were improved. C. B. Meding (Ophthalmology, July, 1913).

Mercury cyanide can be used as diuretic in place of novasurol with equal success. For this purpose it is

necessary to give doses of 0.04 or 0.05 Gm. ($\frac{1}{4}$ or $\frac{1}{8}$ grain), the patient's tolerance having first been ascertained by giving an intravenous injection of 0.01 Gm. ($\frac{1}{16}$ grain). Some investigators have believed that mercury, in inducing diuresis, acts on the kidneys; others, that it influences the body tissues and fluids. Ambard's constant rises markedly after an injection of mercury, and this unfavorable action persists for several days; during the period of diuresis the urine has a very high content of chlorides but a very low one of urea, both in cases with edema and in healthy subjects on a salt-free diet. Again, where diuresis was obtained with ouabain or calcium chloride, the urea output was not reduced, although there was a considerable excretion of chlorides, and Ambard's constant improved. All this suggests that mercurial diuresis is caused through an action on the kidneys; the condition produced is in some respects similar to azotemic nephritis, in which there is reduced urea excretion in conjunction with a normal chloride excretion. While the disturbance of the kidneys by mercury is easily repaired when these organs are in good condition, the drug is contraindicated in dropsies of nephritic origin. L. Blum and H. Schwab (Presse méd., Dec. 16, 1922).

MERCUROCHROME.—This preparation, more specifically known as *mercurochrome-220 soluble*, is chemically the disodium salt of dibromoxymercury fluorescein.

Physiological Action.—Mercurochrome acts both as a germicide and a penetrating dye. It does not precipitate proteins, is not decomposed by urine, and is claimed to be applicable to mucous membranes without producing the irritation which results from the ordinary mercury compounds.

Upon excessive absorption the usual phenomena of mercurial intoxication are produced, *viz.*, soreness of the gums, salivation, loosening of the teeth and diarrhea.

Local Uses.—Mercurochrome is often used in a 1 per cent. solution, but solutions up to 2½ per cent. have been employed. Its germicidal efficiency has been proved in

infections of the throat, nose, sinuses, ear, eye, teeth, etc. A 2 per cent. solution is, according to Weymann, an unusually non-irritating and penetrating, powerful antiseptic for ophthalmic use.

In **anterior urethritis**, after preliminary injection of or irrigation with sterile water or normal saline solution, 1 or 2 drams (4 to 8 c.c.) of the solution are injected and retained for 5 minutes. In **posterior urethritis**, ½ to 1 ounce (15 to 30 c.c.) may be injected through a catheter or with a posterior urethral syringe. The injections are to be discontinued soon after the gonococci have disappeared. Young, White and Schwartz (Jour. Amer. Med. Assoc., July 9, 1921) have emphasized its value in **chronic urethritis, prostatitis and vesiculitis**. Long-standing **chronic cystitis** often clears up after a few treatments. It is less irritating in the renal pelvis than silver nitrate. It makes a good dressing for **venereal ulcerations and buboes**, as well as in **open wounds and sinuses**.

A 4 per cent. solution of mercurochrome is a valuable, non-irritating solution for **sterilizing the birth canal** before labor. The drug is particularly adapted for **induction of labor** and all **operative deliveries**. Mayes (Amer. Jour. of Obst and Gyn., July, 1925).

Mercurochrome stains on the skin can be removed with a solution of chlorinated soda. Stained fabric may be cleared by dipping for 1 minute in 1 per cent. HCl with 2 per cent. potassium permanganate, then in 1 per cent. HCl with 5 to 15 per cent. of U. S. P. hydrogen peroxide solution until the permanganate has been reduced, to be followed by thorough rinsing in water.

Oral Use.—A distinct germicidal effect in the urinary tract can be obtained by giving mercurochrome orally. According to Young, Scott and Hill (Jour. of Urol., Sept., 1924), it causes little or no gastrointestinal disturbance unless taken in large doses a week or more. With a dosage of 0.9 Gm. (14 grains) daily, the urine shows colorimetrically a dilution of 1:30,000 to 1:40,000, or occasionally 1:15,000 to 1:20,000, according to the intake of water. At this strength urine is bacteriostatic. The stools become deeply stained, almost brick red in color, and the normal bacterial con-

tent may be greatly reduced. The drug may have value in infection of the stomach and intestinal tract, eliminating the cause of a urinary infection, colitis, etc.

Intravenous Use.—This mode of administration has been tried in a variety of disorders, chiefly **septic states**. In a review of 255 cases thus treated, including **puerperal sepsis, septicemia, erysipelas, genito-urinary infections, gonorrhea, pneumonia, local infections, typhoid, meningitis, epidemic encephalitis, multiple arthritis, gas gangrene, acute osteomyelitis and psoriasis**, Young (Surg., Gyn. and Obst., Jan., 1925) stated the percentage of recoveries as 42.3; marked improvement had resulted in 38.8 per cent., and failure in 24 per cent. Over $\frac{2}{3}$ of the failures occurred in cases of gonorrhea. The dosage ranged from 1.7 to 7.5 mgm. per kilo. of body-weight, in a 1 per cent. solution. The injection was in some cases repeated at intervals of 1 or more days.

Of 14 cases receiving not over 5 mgm. per kilo. of mercurochrome intravenously, at least 6 of the 10 cases recovering were believed to have been definitely benefited by the procedure. These 6 cases comprised 3 of **puerperal sepsis** and 1 each of **septicemia** following tonsillitis and jugular thrombosis, **gunshot wound** of the chest, and multiple **osteomyelitis**. H. H. Trout (Surg., Gyn. and Obst., May, 1926).

METAPHEN.—This is chemically bis-acetoxymercuri-4-nitro-2-cresol: $(\text{CH}_3\text{CO}\cdot\text{OIlg})_2$: $(\text{C}_6\text{H}_4\cdot\text{CH}_3\cdot\text{OIl}\cdot\text{NO}_2)$. It contains 58 to 60 per cent. of mercury in organic combination.

Physiological Action.—It is a germicide more powerful than mercuric chloride and certain organic mercury compounds when tested on cultures of *Staphylococcus aureus* and *Bacillus typhosus*. It is stated to be relatively non-irritating when applied to mucous membranes or the skin and to be without deleterious action on metallic instruments or rubber. Metaphen is claimed to be relatively non-toxic. White rats were found to tolerate 0.004 Gm. per kilo. intravenously and to tolerate 0.03 Gm. per kilo. intramuscularly.

Therapeutics.—Metaphen is recommended in the treatment of **gonorrhea, ocular and nasal infections, for skin sterilization, and**

for the sterilization of instruments and rubber. Solutions of it in water are prepared with sodium hydroxide. For disinfection of instruments and for application to the skin, solutions of 1:5000 to 1:1000; for ophthalmological use, solutions of 1:15,000 to 1:10,000, and for urethral irrigation, solutions of 1:5000 to 1:10,000 are employed.

C. E. DE M. SAJOUS

AND

L. T. DE M. SAJOUS,
Philadelphia.

METHYL ALCOHOL POISONING.—All the alcohols of the mon-acid series are toxic, though in an ascending scale, from methyl alcohol to amyl. Methyl alcohol (wood alcohol, cologne spirits, Columbian spirits, colonial spirits, eagle spirits, etc.) $[\text{CH}_3\text{OH}]$ is, however, cumulative in its effects, and the others are not. This seems to be mainly due to the fact that methyl alcohol is more slowly excreted and destroyed in the system. It is used as an adulterant and substitute for grain alcohol (ethyl alcohol) in whisky and other alcoholic beverages, lemon and other cooking extracts, essences, and flavoring fluids; in the preparation of many proprietary and patent medicines, e.g., witch-hazel, domestic liniments, bay rum, cologne, and Florida waters, and other perfumes, and in the arts, as in the manufacture of varnishes, for stiffening hats, lacquering brass, etc. The poison may either enter by the mouth, be absorbed by the skin, or be inhaled, in the latter cases producing chronic poisoning by its cumulative effects, and in the first either acute or chronic poisoning, according to the amount taken and the length of time the poison has been used. Partial excretion of methyl alcohol takes place through the lungs and kidneys.

The high toxicity of methyl alcohol after ingestion must be due to chemical changes which occur in the body. Pohl showed that methyl alcohol is changed into formic acid, to which he ascribed the harmful effects. The writer found that formic acid induces in animals the same symptoms as methyl alcohol; it has specific toxic actions, aside from the induction of

acidosis. In poisoning in the dog, sodium bicarbonate in large doses proved very beneficial. H. Leo (Deut. med. Woch., June 26, 1925).

SYMPTOMS.—The symptoms of **acute poisoning** are abdominal pain, general weakness, nausea, vomiting, vertigo, headache, mydriasis, and bilateral blindness. If recovery does not occur, there is a marked depression of the heart action, a sighing respiration, cold sweats, delirium, unconsciousness, coma and death. The blindness may appear in a few hours or be delayed. It is generally complete, with subsequent improvement, and, finally, a relapse into permanent blindness.

The symptoms of **chronic poisoning** are not so pronounced or so easily recognized as those of the acute form. Hyperesthesia and paresthesia of the hands, pain induced by pressure over nerve trunks, and pain in the joints indicate a peripheral neuritis. In a few days absolute blindness usually appears, which follows the course indicated under acute poisoning.

DIAGNOSIS.—Acute abdominal distress, followed by blindness, and perhaps peripheral neuritis, should lead one to suspect this condition.

Variable vision, nausea and vomiting are suggestive. A sluggish, dilated pupil which may or may not react to light or convergence, scleral congestion, deep pain on rotation of the globe, tenderness on finger pressure, and occasionally a temporary paresis of the extra-ocular muscles are typical signs.

PATHOLOGY.—Methyl alcohol appears to have a selective action on the optic nerves, which suffer a destructive inflammation of their fibers or retinal elements (or both), followed by atrophy. The optic outlines are blurred, there is some papillary edema, and the central vessels are engorged. As the acute papillitis subsides vision improves somewhat, only to be followed by postneuritic atrophy and permanent blindness.

TREATMENT.—If the patient is seen within 12 hours after taking the wood alcohol and is not comatose, a **stomach tube** should be passed and the stomach washed out with a 2 per cent. warm solution of **sodium carbonate**, followed by a 50 per cent. solution of **magnesium sulphate**, 3 or 4

ounces of which are left in the stomach. **Warmth** in bed, and 6 doses, 2 hours apart, of 45 grains (3 Gm.) of **sodium bicarbonate** with $\frac{1}{2}$ pint (250 c.c.) of **water** constitute the next steps. The same dose of bicarbonate is then given 3 times a day with a glass of water 1 hour before meals until the symptoms disappear. A **liquid diet** is necessary until then. If there is coma, cyanosis and depressed circulation, stomach washing is not indicated at first. **Fischer's solution** of **sodium carbonate**, 0.37 per cent., and **sodium chloride**, 1.4 per cent., is given intravenously, 1000 c.c. being injected. If there is time, 100 to 300 c.c. of **blood** should be previously **withdrawn**. **Spinal puncture** is sometimes useful to overcome restlessness and cerebral compression. The bowels should be kept free with **magnesium sulphate** (R. Isaacs).

Other measures which have been advocated are **high rectal injections**, to be followed by the use of **pilocarpine**, **hot baths**, **diuretics**, and **potassium iodide** internally; **stimulants**, especially **strychnine** and **coffee**; **alternate hot and cold affusions**, to combat coma, and a **milk diet** for its diuretic action. For the optic nerve condition, **strychnine** may be tried.

Benefit from **lumbar puncture** in 3 cases of methyl alcohol blindness. The improvement followed at once and continued as the punctures were repeated. Zethelius (Hygiea, Jan. 31, 1920).

Early use urged of **sodium bicarbonate** intravenously, guided by Van Slyke's test. In mild wood alcohol toxemia, the writer gives 20 grains (1.3 Gm.) every 2 hours. **Donovan's solution** recommended as an eliminant, and **pilocarpine** to stimulate lymphatic activity. **Lavage**, **emetics** and **diaphoretics** are helpful to promote elimination, but strychnine has not proven of value. The optic nerve should be stimulated with **negative galvanism**. Ziegler (Penna. Med. Jour., Dec., 1921).

Blindness due to methyl alcohol may occur not only after acute intoxication but through the cumulative effects of small amounts. In the former instance, no disturbance of sight may be

noticed at first, but several hours later severe gastrointestinal symptoms may appear, together with rapid failure of vision. This may proceed to complete blindness, and pronounced pupillary dilatation may occur; usually, however, marked improvement of vision takes place for several days, after which visual failure sets in again and ends in permanent blindness. In this second stage treatment is of no avail. The early treatment consists of gastric lavage continued for days, sweating with Turkish baths or pilocarpine, venesection, alkalies, and in severe cases, lumbar puncture. J. M. Downing (Jour. Iowa State Med. Soc., Nov., 1922).

W. and S.

METHYL AND METHYLENE CHLORIDES.

Methyl chloride (monochloromethane; chloromethyl) [CH_3Cl] is a gaseous compound obtained by the reaction between methyl alcohol and hydrochloric acid in the presence of zinc chloride, with subsequent purification. It occurs as a colorless gas with a sweet taste and an ethereal odor, soluble in $\frac{1}{4}$ its volume of water, much more so in alcohol, and freely in ether and chloroform. It is less inflammable than ether. Under a pressure of 5 atmospheres at normal temperature it becomes a neutral liquid, which has been recommended for use as a spray to relieve pain and itching in severe neuralgia and pruritus, and to produce local anesthesia. The surface should previously be anointed with petrolatum to prevent the formation of blisters.

Methylene chloride (methylene bichloride; dichloromethane; chloromethyl) [CH_2Cl_2] is obtained by the reduction of chloroform (in alcoholic solution) by zinc and hydrochloric acid, with subsequent purification. It occurs as a heavy, colorless liquid, boiling between 104° and 105° F. (40° and 41° C.), and having an odor suggesting that of chloroform. It is soluble in alcohol and ether, and is decomposed when exposed to light and air, the change being prevented by the addition of a little alcohol.

Methylene bichloride has been proposed for use as a general anesthetic safer than chloroform. Its high cost, however, militates against its employment, and, fur-

thermore, it is doubtful whether this compound is not even more dangerous than chloroform. One fluidram (4 c.c.) inhaled every five minutes is the average quantity required for producing anesthesia. It may be used internally in doses of from 5 to 15 minims (0.3 to 1 c.c.).

W. and S.

METHYLENE BLUE.—Methylene blue [$\text{C}_{16}\text{H}_{18}\text{N}_3\text{SCl}$] is one of the aniline dyes, a diphenylamine compound resulting from the action of hydrogen sulphide upon an oxidation product of para-amidodimethylaniline. It occurs as a fine, dark-green crystalline powder or in crystals, readily soluble in water, less readily in alcohol, the solutions having a deep-blue color. A solution of methylene blue cannot be distinguished from a solution of methyl blue or methyl violet (pyoktanin) without great care, and toxic effects have been observed as a result of errors in prescribing the one drug for the other, the dose of pyoktanin being smaller.

Tests to distinguish methylene blue from methyl blue are as follows: 1. The meniscus on the surface of a solution of methylene blue in a test-tube, or a thin film of such a solution, has a greenish color, while that of methyl blue is blue under all circumstances. 2. When sodium hydrate is added to a solution of each the color of the methylene-blue solution is changed to violet, while that of the methyl blue becomes a reddish brown (Smith). 3. A diluted solution of methyl blue becomes decolorized on the addition of ammonia water, while a solution of methylene blue (even if very highly diluted) is not decolorized.

PREPARATION AND DOSE.—*Methylthionina chloridum*, U. S. P. (methylene blue). Dose, 1 to 4 grains (0.06 to 0.25 Gm.); official average dose, $2\frac{1}{2}$ grains (0.15 Gm.).

MODES OF ADMINISTRATION.—Methylene blue, when used orally, is best given in capsules or cachets. Nutmeg may be combined with it to prevent gastric and cystic irritation. When it is used by injection, the dose is from 1 to $1\frac{1}{2}$ grains (0.06 to 0.1 Gm.), and the solution should always be boiled before use to prevent abscess formation.

Commercial methylene blue contains zinc, and therefore may cause vomiting.

PHYSIOLOGICAL ACTION.—Externally, methylene blue is antiseptic and analgesic.

In guinea-pigs the giving of a toxic dose of methylene blue is followed, according to Combemale, by a marked increase of the reflexes and of the respiratory rate, with subsequent motor paralysis and death. At the necropsy there is found a chocolate discoloration of the blood, caused by a destructive action upon the red blood-corpuscles, flaccidity of the heart, pulmonary atelectasis, and engorgement of the liver, with blue discoloration of the biliary ducts and of the gastric and intestinal mucous membrane. Lauder Brunton and Delépine subsequently observed that the drug sometimes causes a great accumulation of iron in the liver.

Experiments on frogs and rabbits by Mikhailoff have shown that the leucocytes do not fix methylene blue until a short time before death, and even then only rarely. At the autopsy of the animals experimented upon for a period of three weeks there was found in all the serous cavities a blue liquid; all the organs were also colored; the blood was methemoglobinized, the result being a loss of oxygenation, which had led to degeneration of the parenchyma and favored thrombosis.

Lemanski and Main have found that methylene blue can be detected in the saliva forty minutes after its introduction by the mouth, and in one hour and fifteen minutes after its use by the rectum.

Elsner has estimated by colorimetric methods the amount of methylene blue excreted from the body in the urine and intestines. In 4 cases the total quantity excreted averaged 68 per cent. of the quantity ingested.

Müller found that with normal kidneys the remedy first appears in the urine twenty minutes after its intramuscular injection, the elimination reaching its maximum in about one and three-quarter hours, then gradually diminishing. Slight retardation was noticed in cases of interstitial nephritis, and acceleration in a case of chronic parenchymatous nephritis.

THERAPEUTICS.—Methylene blue being eliminated by the urine, Achard and Castaigne conceived the idea of using this property to determine renal permeability

when disease of the kidney is suspected. To test the eliminative function of the kidney, 1 grain (0.065 Gm.) dissolved in 10 minims (0.6 c.c.) of water is injected into a muscle. If the kidneys are normal the urine should show a greenish discoloration in from fifteen to thirty minutes, and continue discolored for thirty-six hours.

In *diabetes mellitus* methylene blue appears to act somewhat like antipyrin. After its administration in full doses, up to 6 grains (0.4 Gm.) three times daily for six weeks, sugar has been found to disappear from the urine.

Stucky has obtained good results from this drug in *vesical irritability* and *cystitis*, particularly in cases of enlarged prostate in the aged.

Lemoine employed methylene blue in 8 cases of *albuminuria*. In 5 there followed a rapid diminution and in 3 a complete disappearance of the albumin. The doses employed varied from $\frac{1}{8}$ to $\frac{3}{4}$ grain (0.02 to 0.05 Gm.) a day.

The property of methylene blue of staining the axis cylinders of nerve suggested to Ehrlich that it might prove useful as analgesic in painful neuroses, including *neuralgia*. It was found effective at times both in this condition and for reducing the pain of *migraine*, *herpes*, *rheumatism*, and *sciatica*. Of 27 cases of *sciatica* in which Klemperer used methylene blue, in 6 cases the pains disappeared in five days. In 8 cases no effect whatever was observed. About 7 grains (0.5 Gm.) were given daily.

Combemale obtained complete relief with it in the *neuritis of alcoholism*, of *tabes* in the second period, and in *bone pains of tuberculous, syphilitic, and traumatic origin*. The drug was usually given in doses of 3 grains (0.2 Gm.) a day. The untoward effects most commonly, although not frequently, observed were headache, nausea, and diarrhea.

Armstrong finds methylene blue particularly valuable in those forms of *rheumatoid arthritis due to autointoxication from the intestinal tract*.

Zaitzev and Torporkov found methylene blue useful in severe *psychoses accompanied by marked insomnia*, in doses varying from a fraction of a grain, given hypodermically, to 2 or 3 grains (0.13 to 0.2 Gm.) by the mouth. Hughes and Lovelace used

it in 22 cases of various forms of **mania** and **paretic dementia**, in all of which wild excitement existed. In all but 6 cases it produced a calmative effect, "a natural quietude, unlike the sedative action of other drugs," coming on three or four hours after a dose was given and lasting for from fifteen to twenty-four hours. Generally 1 grain (0.06 Gm.) was given twice daily or oftener, hypodermically; in some instances double this dose in capsule. (To avoid abscesses the solution should be boiled before injection.) Bodoïn tried methylene blue in 14 cases of cerebral excitement, including **mania**, **paranoia with delirium**, **chronic alcoholism**, and **hysteroepilepsy**, and found its use very satisfactory when it was injected into the gluteal muscles in doses of from 1 to 1½ grains (0.06 to 0.1 Gm.). Its quieting effects continued from one to four days. There were no untoward effects.

Pain and odor are frequently removed when methylene blue is injected in the dose of 1 grain (0.06 Gm.)—in aqueous solution—directly into inoperable **cancerous growths**. At times an inhibitory action on the tumor has also been noted.

In **malarial fevers** Guttman and Ehrlich, basing their opinions upon the fact that methylene blue stains the hematoozon, were led to consider this agent as of value. The remedy was also tried with apparent success by Thayer in doses averaging 1½ grains (0.1 Gm.) five times a day. The only untoward effect produced was stranguary; this was relieved, however, by the ingestion of an equal quantity of nutmeg, and did not appear at all where nutmeg was given from the beginning. On the whole, though effective in malaria, methylene blue is inferior to quinine or arsenic. It is worth a trial, however, where quinine is not well borne. In **malarial hematuria** it gave Stucky better results than any other remedy. He administers it in doses of 3 grains (0.2 Gm.) three times daily until the urine becomes decidedly blue.

Reichmann has advised the administration of ½- to ¾-grain (0.03 to 0.05 Gm.) doses of methylene blue in inflammatory disorders of the liver, such as **cholangitis** and **cholecystitis**. Bauer has detected considerable amounts of the drug in the bile.

O'Neil asserts that methylene blue will cure **gonorrhea** in from four to seven days,

being a drug especially fatal to diplococci and pyogenic bacteria. He advises that it be given in gelatin capsules in 1-grain (0.06 Gm.) doses, combined with 1 drop of nutmeg oil and 2 drops of sandal oil, three or four times a day. After the fourth day the dose may be administered twice a day.

According to Chaleux and others, methylene blue in concentrated solution, or powder, is useful in the treatment of **metritis**, being painless and non-toxic. It quickly arrests **metrorrhagia** and **menorrhagia** and diminishes **leucorrhœal** discharges. It sometimes removes pain in **dysmenorrhea** accompanied by changes in the uterine mucosa.

Local use of methylene blue in **Oriental sore** has been advised by Billet. For **Vincent's angina**, the following is recommended:—

R. *Methylthionine chlori*

ridi gr. xlv (3 Gm.).

Glycerini,

Alcoholisââ gr. lxxv (5 c.c.).

M. Sig.: To be painted over the membrane-covered areas. W. and S.

MIDDLE EAR, DISEASES OF.

—The four generally recognized divisions of middle-ear disease are *acute catarrhal otitis media*, *acute suppurative otitis media*, *chronic suppurative otitis media*, and *chronic catarrhal otitis media*. An exact scientific classification of these diseases is impossible, for the reason that every degree or stage, from the simplest catarrh to the severest form of inflammation, may occur successively in the same attack. A mild catarrh may rapidly become a severe inflammation or suppuration, whereas the acute inflammatory state may abate and subsequently assume the simple catarrhal form. It is impossible to state definitely where an acute catarrhal process ends and the acute suppurative lesions begin.

The term "catarrh" obviously can be used only in connection with an abnormal state of a mucous mem-

brane, such as the lining membrane of the middle ear, and never in a similar condition of skin surface, such as that covering the external auditory canal. Middle-ear or tympanic catarrh indicates a mild, simple inflammation of its mucosa, without serious involvement of the underlying structures and little or no systemic disturbance, but showing a pronounced tendency to resist treatment. An acute suppurative inflammation of the same cavity represents the more violent, and in some instances virulent, forms of pathological changes of the mucous membrane, resulting frequently in destruction of the mucosal lining, thus exposing the osseous structure to the ravages of the pathogenic organisms found in the consequent mucopurulent or purulent discharge. It is usually accompanied by systemic disturbance. Under prompt and proper care, this disease usually ends in recovery, without any special predisposition to relapse, but without such care it is the most dangerous of aural affections. Its importance can be forcibly brought out by the further statement that practically all serious ear affections and their complications, such as diseases of the mastoid process, sinus thrombosis, meningitis, labyrinthitis, and brain abscess, originate in an inflammatory process within the tympanic cavity. Not too much stress, therefore, can be laid on the necessity of *prompt* treatment in the initial stage of this seemingly simple aural disease, in view of the dangerous complications to which neglect or procrastination may give rise.

The etiology of the catarrhal and suppurative forms of otitis media is identical; the symptoms, both object-

ive and subjective, are similar, varying only in degree, up to the point of perforation. Before perforation the condition is regarded as catarrhal; afterwards, suppurative, and in the absence of proper care at this stage the disease assumes the character of an acute or chronic suppurative otitis media, with all its potential dangers. Inflammatory aural conditions complicating the exanthemata, influenza, pneumonia, and typhoid fever present early symptoms of such severity that they are considered purulent from the beginning, and in such cases an early incision of the membrana tympani for evacuation of the pus is most necessary.

To summarize: Catarrhal and suppurative otitis media present practically the same picture at onset. If the symptoms, however severe, yield without perforation or incision of the membrana tympani, the case may be regarded as catarrhal in nature; but if the destructive activity of the infection causes necrosis and maceration of the tympanic mucosa, with consequent perforation and discharge, then there exists a purulent inflammation, *i.e.*, an acute suppurative otitis media.

A brief survey of the more important anatomical points will give a better understanding of the pathological changes occurring in aural disease. The mucosa covering the nasopharynx acts also as a mucous lining for the Eustachian tube and middle-ear cavity, and, being greatly modified, forms the internal layer of the membrana tympani. It likewise covers the ossicles, and, finally, serves as the protective covering of the mastoid antrum and cells. Because of this intimate mucosal relationship,

it will readily be appreciated how easily, by continuity, an inflammatory process of the throat or nasopharynx can involve the middle ear and adjacent structures by way of the Eustachian tube. The same is true, in a less degree, of the external auditory canal, with the exception that this is covered with a skin reflected from the auricle, which eventually forms the external layer of the *membrana tympani*. The notably thin bony framework of the middle-ear cavity is surrounded by some of the most vital structures in the human economy. The roof of this cavity, always thin, is in some instances entirely absent, particularly in young children and infants. The carotid canal, through which passes the carotid artery, forms the anterior wall; the jugular fossa, in which lies the bulb of the jugular vein, constitutes the floor, while the roof is formed by the floor of the middle fossa of the skull, on which rests the temporosphenoidal lobe of the cerebellum. Above and behind the oval window, on the internal wall, is situated the Fallopian canal, which contains the tympanic branch of the facial nerve. The bony wall separating the lateral sinus from the mastoid cells is also thin to the point of translucency.

The foregoing facts make it apparent with what facility the meninges may be implicated through the roof, or the jugular vein through a dehiscence or carious erosion of the floor. The labyrinth, or nervous part of the organ of hearing, may likewise be involved by erosion through the internal tympanic wall. It should be noted also how easily Bell's palsy may be caused by injury to or disease

of the tympanic branch of the facial nerve, as may likewise a greater or less disturbance of the equilibrium should the middle-ear disease extend to the semicircular canals.

While the tympanic cavity and the mastoid antrum and lower cells are spoken of as distinct and separate cavities, the latter are, in reality, accessory to the former, being separated from it by a comparatively narrow space. Herein is afforded an explanation of the usual involvement of the mastoid process, to a greater or less extent, in practically all acute inflammatory disease of the middle ear.

Otitis media in infants deserves special mention from the fact that the petrosquamous suture provides free communication between the lymphatics and blood-vessels of the tympanic cavity and the interior of the skull. On account of this relationship, children frequently develop an otitic meningitis or other intracranial complication without even giving evidence that an aural lesion is present. Many cases of this type have come under my care, the underlying cause of the meningitis never having been suspected until, by accident or the appearance of a discharge from the external auditory canal, the real cause of the infant's illness was discovered. In proof of this one need only mention that Ponfick, in post-mortem examinations of 100 cases in which the ear was not suspected in life, found otitis media in 90 per cent. of infants under 3 years of age.

ACUTE CATARRHAL OTITIS MEDIA (Otitis Media Acuta Catarrhalis).

DEFINITION.—An acute non-suppurative inflammation of the middle ear.

SYMPTOMS.—In the more simple forms of infection the patient experiences only a fullness or dullness within the ear and a slight impairment of hearing. In the exaggerated type the pain is more or less severe and the loss of hearing becomes much more marked. The latter symptom is especially prominent at night. Indeed, the patient may be relatively free from all symptoms during the day, but suffer greatly from nocturnal pain. The above symptoms characterize what is termed "earache in children," to which, unfortunately, only too often little attention is paid. The pain is not confined to the ear itself, but is frequently complained of as a headache, more marked on the affected side, radiating toward the teeth, the patient especially complaining on opening the mouth and when pressure is made on the tragus. A rise of temperature is usually a matter of considerable importance, particularly in children. In some instances, however, even when the involvement is serious, the patient has very little fever, or, indeed, little, if any, inconvenience. The symptoms are so mild and seemingly unimportant, in some cases, that they do not attract attention; this shows the importance of an aural examination when the exact cause of an illness cannot be definitely determined, especially in children. Again, the temperature in children may be high, ranging from 103° to 105° F. A temperature of this height, while not usually indicating a serious complication in infants, should always be viewed with grave apprehension in an adult. In those too young to speak or otherwise indicate the location of the pain, the hand is fre-

quently raised to the ear or in the direction of the affected side. This should always make us suspicious of aural involvement in infants.

The intensity of the pain is governed by the severity of the inflammation, or, more especially, by the pressure exerted on the inflamed mucosa and drumhead by the amount of exudate or great retraction of the drumhead. This explains why the pain in acute catarrhal otitis media, with little exudate, is much less severe than that in acute suppurative otitis media, with a copious exudate.

Tinnitus aurium, which is present in most cases, causes distress to the patient when severe, and especially when it is pulsating in character. The tinnitus may resemble any form of noise, but is usually of the rushing, singing, or hissing type. That resembling the escape of steam seems to be particularly annoying.

The degree of deafness is governed almost entirely by the site of the exudate. The tympanic cavity may be well filled with fluid and yet the hearing remain fairly good, but if the exudate clogs both the round and oval windows the deafness may be very great. Hallucinations of hearing are not infrequent.

Repeated attacks of catarrhal otitis media (subacute catarrhal otitis media) in early life result in changes in the membrana tympani, as well as adhesions, which in later life are the cause of more or less deafness. This illustrates the importance of prompt treatment in all such cases, that there may be fewer instances of chronic deafness in future generations.

The duration of the disease varies from two to ten or twelve days. In mild cases the membrana tympani is

congested, more especially in the superior part, the process also extending along the long handle of the malleus. In the severer types the entire drumhead is red and swollen, owing to infiltration of the dermal layer. The landmarks (the long handle and the short process) are more or less obliterated, the former being obscured first. When bulging is present, it usually appears first in the superior and posterior quadrant or the posterior and inferior quadrant. As resolution begins, the congestion slowly disappears, Shrapnell's membrane and the long handle of the malleus being the last to recover.

As the secretion incident to the nasopharyngeal disease increases, there is a correspondingly increased full or stuffy feeling in the ear. This is caused by the pharyngeal end of the Eustachian tube becoming involved and finally blocked by the secretion,—nature's method of sealing off the communication between the nasopharynx and the middle ear, the entrance of infectious micro-organisms being thereby prevented. This stuffy feeling, therefore, should be borne for two or three days and no special attempt made for its relief; if the protective barrier is broken through by either blowing the nose or the use of Politzer's method of inflation, the chances of inducing an infective otitis media are very great. This illustrates forcibly the importance of never inflating an ear during the early stage of an acute inflammatory disease.

ETIOLOGY.—The most common cause of middle-ear catarrh is an extension, by continuity, of a similar process from the nasopharynx through the Eustachian tube into the middle ear.

This catarrhal condition is usually greatly aggravated by the presence of diseased tonsils and adenoid vegetations in children and by nasal obstruction in adults. The immediate cause in the usual case, therefore, is what is ordinarily termed a "cold in the head," or acute coryza, regardless of what the underlying etiological factor may be. Additional exciting causes are the unwise and dangerous practice of the use of the nasal douche and the snuffing up of various solutions; also sea-bathing and dentition in children. As blowing the nose during an attack of coryza is one of the chief causes of middle-ear infection, it should be rigorously avoided, especially when both nostrils are closed, as in the usual method of clearing the nose; in other words, one nostril should always remain open during this procedure.

The diseases which not only cause a catarrhal inflammation of the middle ear, but one apt to become rapidly suppurative, and indeed credited with being suppurative from its inception at times, are measles, scarlatina, diphtheria, pneumonia, typhoid fever, and influenza. The first- and last-named affections are probably productive of more serious aural disturbance than all other diseases combined. This is especially true of influenza, as is shown by the fact that before its advent tympanic and mastoid inflammation requiring operative intervention were comparatively rare, whereas at present these are among our most common diseases. Whooping-cough, bronchitis, and parotitis, as well as inflammation conveyed by means of the lymphatics and general circulation, are additional causative factors in middle-ear disease.

PATHOLOGY.—The mucosa becomes hyperemic and more or less swollen, according to the severity of the inflammatory process. The amount of the accompanying secretion is likewise governed by the degree of inflammation. When the entire mucous membrane is involved, the secretion is abundant, and when it is serous in character the condition is known as *serous catarrh*. When the inflammation and consequent

pressure exerted from without. Cases of this type are sometimes more painful than the acute suppurative form.

PROGNOSIS.—In the less severe cases the prognosis is always good when treatment is prompt. In the severer types, especially those complicating the exanthemata, pneumonia, and typhoid fever, the prognosis, although favorable, should be more guarded.

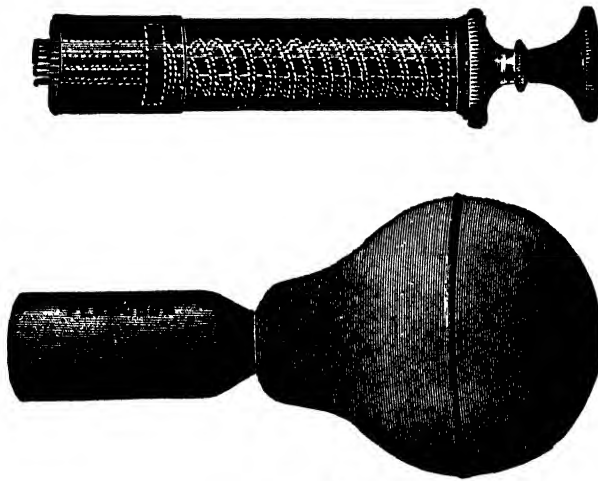


Fig. 1.—Artificial leech.

secretion are confined to the pharyngeal end of the tube, without involvement of the middle-ear cavity, the condition is known as *tubal catarrh*. *Hydrops ex vacuo*, or a collection of practically non-inflammatory fluid in the middle ear, is the result of a slowly developing tubal catarrh, with extension into and final involvement of the tympanic cavity. If the Eustachian tube remains blocked on account of the swelling of its mucous membrane, the middle ear becomes a closed cavity. The subsequent absorption of the air within results in great retraction of the membrana tympani, owing to the atmospheric

TREATMENT.—So far as possible, one should remove the cause, such as diseased tonsils and adenoids, nasopharyngeal catarrh, and nasal obstruction of any type that may interfere with free nasal respiration. The patient should be confined to bed, or at least to an equable temperature, and placed on a restricted diet. The bowels should be freely opened, and small, frequently repeated doses of tincture of aconite administered. In the early or hyperemic stage blood-letting by means of the natural or artificial leech (Fig. 1), preferably the latter, in front of the tragus is of distinct benefit. At the inception of

the disease, the **instillation** of, or **irrigation** by, **warm** solutions will frequently abate an attack of acute catarrhal otitis media. For this purpose a **normal salt solution** or **saturated boric acid solution** may be used. In the very mild cases the aural pain will be promptly relieved by instilling hot boric acid solution into the ear and allowing it to remain for about five minutes, a piece of hot flannel being placed over the ear to retain the heat. Equal parts of **tincture of opium** and **tincture of belladonna**, or a 5 to 10 per cent. solution of **phenol** in glycerin, properly heated, will answer a similar purpose; this is to be repeated, if necessary, 3 or 4 times a day. A 5 to 10 per cent. solution of **cocaine** is credited with being of benefit in some cases.

Since our chief object in treatment is to restore the patency of the Eustachian tube and rid the tympanic cavity of secretion, it is necessary to employ **inflation** by means of **Politzer's method** (Fig. 2) as early as possible. This should never be done, however, until the acute inflammatory symptoms have subsided, which, in the average case, will be in two or three days after the last vestige of pain has passed. Force should never be used in inflating the ear, and this is avoided by placing a few drops of chloroform in the bag. If inflation does not cause pain, it should be repeated every two or three days until the hearing has been restored. It is important to remember that *force should never be used*.

If the disease subsides under the above treatment, even though considerable fluid may have accumulated in the tympanic cavity, it is still regarded as a catarrhal otitis media.

If, however, it is necessary, on account of the accumulation of fluid, to incise the drumhead, or if the membrana tympani has ruptured spontaneously, the case is then known as an acute suppurative otitis media, the treatment of which will be taken up under that heading.

ACUTE SUPPURATIVE OTITIS MEDIA (Otitis Media Acuta Purulenta).

DEFINITION.—An acute suppurative inflammation of the middle ear.

SYMPTOMS.—The earlier symptoms are those of an acute catarrhal



Fig. 2.—Poltzer bag.

otitis media up to the point of perforation, in the average case. In some instances the attack seems to be suppurative from its inception. The symptoms are then greatly exaggerated, the pain being intense and continuous, and radiating over the entire side of the head. In extreme cases the suffering is so acute and the temperature so high that in conjunction with the changed mental attitude the picture resembles one of meningitis.

In all acute suppurative conditions of the middle ear the mastoid process is involved to a greater or less degree, and accordingly there is usually some tenderness about the ear and over the mastoid process. The labyrinth is also involved occasionally, as is manifested by attacks of

vertigo and tinnitus aurium. Impairment of hearing is usually well marked. As a rule, one ear is involved, but both ears frequently are affected during an attack complicating the exanthemata or influenza.

Spontaneous perforation of the membrana tympani may occur from the first to the fourth day in the more virulent forms of infection, or may not occur for ten days or two weeks in the milder cases. Usually great relief follows the evacuation of the pent-up secretion, the pain and fever subsiding simultaneously. If this improvement is not shown, however, and the symptoms above enumerated continue, there is great probability of more serious involvement. The profuse discharge lasts from one to two weeks, after which it gradually subsides, usually ceasing in the third or the fourth week.

In addition to the hyperemia and swelling of the membrana tympani, the redness is more intense, and as the fluid accumulates the membrane bulges,—a certain indication (in some instances a late sign) for incision of the membrane. If spontaneous perforation has occurred, pulsation synchronous with the heart's action is seen through the membrane, and this is quite characteristic of acute tympanic suppurative. On account of the extreme congestion, greater or less ecchymosis, and macerated epithelial débris, it is most difficult to determine where the external wall ends and the membrana tympani begins. The perforation may be situated in any part of the membrana tympani, and ranges from the size of a pinpoint to that of a small bean, or may even extend to total destruction of the membrane. The larger

perforations are apt to occur in cases complicating the exanthemata.

ETIOLOGY.—The etiology of this disease is the same as that given under acute catarrhal otitis media. In addition, infection frequently arises through extraction of foreign bodies from the external auditory canal, and from injuries. In view of the fact that the caliber of the Eustachian tube is relatively larger in young children than in adults, it must be remembered that a suppuration of the middle ear may actually take place without perforation of the membrana tympani, the fluid escaping under more or less pressure by way of the tube into the nasopharynx. This, no doubt, explains why the severe pain of an acute otitis media frequently subsides without apparent cause, only to return again, in the average case, as the tympanic cavity refills and pressure is exerted on the inflamed mucous membrane. This process may be repeated several times, the case eventually recovering without perforation of the drumhead. Those attacks complicating the exanthemata, typhoid fever, and pneumonia are especially prone to become suppurative and should, therefore, be anticipated and detected by an early examination.

PATHOLOGY.—In addition to that given under acute catarrhal otitis media, the pathological changes are simply those incident to the advanced stage of the disease. When the mucous membrane lining the tympanic cavity becomes greatly inflamed and edematous, and pressure from accumulated fluid increases, the mucosal covering becomes macerated and frequently peels off, exposing the unprotected underlying osseous struc-

ture to the ravages of the various micro-organisms. Herein lies the starting point of carious erosion in various directions, leading to the subsequent establishment of intracranial lesions.

PROGNOSIS. — Uncomplicated suppuration ends usually, under prompt care, in complete recovery, both as regards a cessation of discharge and restoration of hearing to about normal. If ankylosis of the ossicles has taken place, with adhesions between the membrana tympani and tympanic wall, impairment of hearing, as well as tinnitus aurium, will be present. A permanent perforation may also be the cause of some loss of hearing. Complications liable to occur during an attack of acute suppurative otitis media are enlargement of the cervical glands,—rather common in children,—acute mastoiditis, acute involvement of the internal ear, facial palsy, sinus thrombosis, and intracranial complications, such as meningitis and brain abscess formations.

TREATMENT.—In the mild type of case it is best to try to reduce the inflammation by the application of

and although the rule still prevails, in the usual case, to wait until the drumhead bulges, this is a late and unsafe indication in acute suppuration of the middle ear complicating the exanthemata and influenza. It is

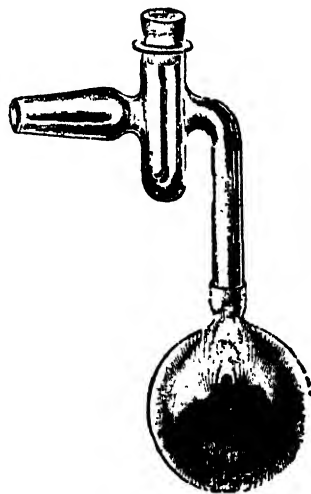


Fig. 4.—Aspirator.

best, therefore, in all severe infections to incise the membrana tympani early, as this is our best means of preventing additional complications.

When the case is seen sufficiently early, the drumhead should never be allowed to rupture spontaneously, as it is in such cases that complications most frequently occur. In the event of a spontaneous rupture (and this only too frequently happens), if the opening is small or situated high up, so that drainage takes place by means of overflow, the opening should be enlarged.

Before incision of the membrana tympani is undertaken, the same thorough surgical preparation, both for patient and operator, must be observed as in major operations, such as that upon the mastoid process.

Free evacuation of pus from the

Fig. 3.—Myringotomy knives, sharp and blunt pointed.

treatment as outlined under acute catarrhal otitis media. When this fails promptly to abate the symptoms, one's efforts must be directed toward the establishment of **free drainage** and the **prevention of various complications**. The most important procedure, therefore, is the early and free **incision of the membrana tympani**,

tympanic cavity can never be accomplished by a simple puncture or paracentesis of the membrana tympani. The membrane must be freely incised, the chief requisite being to carry the incision from the most dependent part downward to the lower border of the canal, said incision to be continued either in an anterior or posterior direction until about one-fourth of a circle has been formed (Fig. 3). This will not only provide for good drainage, but will insure patency of the opening long enough to admit of proper after-treatment. Following a free incision, **aspiration of the tympanic cavity** is advisable, as this will relieve the congested

The local treatment is usually of two types, known, respectively, as the "wet" and "dry" methods. It is necessary to employ the *wet method* in those cases that cannot be more or less constantly under the physician's care, and also where the discharge is profuse. The wet method consists of the use of various **warm medicated solutions**, by means of a **syringe** or **irrigation bag**, or the **instillation** of drops into the ear.

After the establishment of drainage, the more simple cases will improve upon **removal of all secretion** by means of cotton on a cotton-carrier (Fig. 5) or the syringe (Fig. 6), after which a **warm saturated boric**



Fig. 5.—Applicator.

mucosa of considerable blood and thoroughly evacuate the pent-up secretion.

Although incision of the membrana tympani can be performed under **local anesthesia**, it is always better to administer **general anesthesia** when possible. **Nitrous oxide gas** can be employed for this purpose to great advantage. **Ether** still remains the safest and most popular drug for general anesthesia. If for any reason it is desirable to use local anesthesia, the drumhead can, in some instances, be thoroughly anesthetized by applying to the same a solution composed of equal parts of **cocaine, menthol, and phenol**. A small piece of cotton may be moistened with this solution and placed against the membrana tympani, where it should remain fifteen minutes before the drumhead is incised. The patient should be kept in **bed**, given a **light diet**, and **freely purged**.

acid solution should be instilled into the ear and allowed to remain five minutes. This should be repeated every three hours. Should this simple treatment fail, astringent solutions are indicated, such as **zinc sulphate, copper sulphate, or lead acetate**, in the proportion of 5 to 8 grains (0.3 to 0.5 Gm.) to the ounce (30 c.c.) of water. **Silver nitrate**, 5 to 10 grains (0.3 to 0.6 Gm.) to the ounce of water, is especially efficacious in some cases. Where the discharge is persistent, the efficiency of the treatment will depend somewhat on a more or less frequent change of the medication.

The *dry method* of treatment can only be instituted when the acute inflammatory stage subsides, and where the perforation is large and the discharge not abundant. It consists of wiping out the secretion with some antiseptic solution and then dusting the surface with impalpable powder

by means of a powder blower. For this purpose **boric acid** or **aristol** is usually employed, or a combination of both in equal parts. Care should be taken only to *dust* the surface with the powder, as any excess will interfere with free drainage.

Every effort should be made, by **internal medication**, **diet**, and **out-of-door life**, to improve the patient's general health.

Hydrogen dioxide solution, diluted $\frac{1}{2}$, proved the most efficient irrigating fluid. A long, clean incision is necessary for effective irrigation. No case of mastoiditis developed in 75 acute and chronic cases irrigated with this agent. D. T. Smith (Amer. Jour. Dis. of Childr., July, 1924).

After the acute symptoms have subsided, one should **inflate** the middle ear 2 or 3 times a week, gradually decreasing the frequency, and finally ceasing as hearing improves.

CHRONIC SUPPURATIVE OTITIS MEDIA (Otitis Media Chronica Purulenta).

DEFINITION.—A chronic purulent inflammation of the middle ear.

SYMPTOMS.—The chief characteristic of chronic suppurative otitis media is that the patient does not ordinarily complain of pain, but has a more or less constant discharge from the external auditory canal. A discharge mixed with blood-corpuscles indicates the presence of granulations or polypi. If it be brownish or brownish yellow in character, with a fetid odor, there is in all probability caries and necrosis of the bony structures of the tympanic cavity, antrum, or mastoid cells. A profuse discharge strongly indicates involvement of the mastoid process.

So long as the perforation is large and the discharge is not obstructed

by granulations or polypoid growths, the patient suffers no inconvenience, and may, therefore, continue in this state for years without any annoyance except that of a "running ear." If for any reason, however, the discharge becomes obstructed in its egress either from the mastoid process or the middle ear, the patient will probably have a rise of temperature and will suffer from headache or a feeling of heaviness and fullness in the head, or pain in the ear, all of which may continue for a time and be relieved on the reappearance of the discharge.

A perforation situated in Shrapnell's membrane indicates a disease of



Fig. 6.—Ear syringe.

the attic as well as involvement of the ossicles. When located in the superior and posterior quadrant, it is usually associated with disease of the antrum or mastoid cells and the ossicles. If located in the anterior and inferior quadrant, it indicates catarrh of the Eustachian tube or disease of the osseous structure around the tympanic orifice of the tube.

Cholesteatomatous masses are sometimes found within the tympanic and mastoid cavities. Such a mass is composed of an accumulation of desquamated epithelium from the lining membrane. A *cholesteatoma* somewhat resembles an onion in shape and formation, is grayish white in color, and can be peeled off like an onion. The probabilities are that bone necrosis has something to do, also, with the formation of

cholesteatoma. Cases of this type seldom recover without operative intervention.

The hearing is always somewhat impaired, and occasionally markedly so. The average case hears better while the ear is actively discharging, provided the secretion is not too abundant. This is probably due to the fact that the secretion favors the conduction of sound waves.

Unless suffering is present or some other condition arises, such as a sudden facial palsy, an intracranial complication, or a septic infection of the lateral sinus, the average case, untreated, will continue indefinitely.

ETIOLOGY.—As already stated, an acute suppurative inflammation of the middle ear is a continuation of an acute catarrhal process. A chronic suppurative process is likewise a continuation of an acute suppurative otitis media. The acute form of suppuration is frequently due to neglect or inefficient treatment of the catarrhal stage. It is also true that a chronic otorrhea is usually the result of neglect or inefficient treatment of the acute suppurative form. However, there are a good many general causes which tend to prolong the disease, such as pneumonia, syphilis, tuberculosis, diabetes, insufficient food, and unhealthful surroundings. For these reasons, chronic middle-ear suppuration is more common among the poor than the well-to-do.

PATHOLOGY.—Owing to the extensive round-celled infiltration, due to chronic inflammation, the mucous membrane is greatly thickened. Some parts of this membrane are swollen, while others are denuded of epithelium, the result being erosion, ulceration, peeling off, and exposure of the

bone, with consequent caries and necrosis. As the inflammation subsides, new connective tissue has a tendency to bind the ossicles together, causing complete ankylosis, and adherence of the ossicles and fragment of drumhead to the tympanic wall. Granulations and polypi frequently result from local proliferation of the tissues. The mastoid process, the labyrinth, or the interior of the skull may all become secondarily involved.

PROGNOSIS.—The prognosis in chronic suppurative otitis media is always problematical. Even when a discharge has ceased without operative intervention, one can never be certain that it will not recur. Indeed, it is from the recurrent type of case, even though the discharge may have ceased for some months or even a few years, that the majority of the cases of intracranial complications arise. On the other hand, if the discharge has ceased, under treatment, before extensive carious erosion has taken place, and the patient is healthy, the prognosis is favorable. It must not be forgotten, however, that an occasional case will discharge continuously or recurrently for a number of years and then permanently cease suppurating after the discharge of a small sequestrum; but it is always a dangerous procedure to wait for such an occurrence.

TREATMENT.—For success in treatment, each case must be considered separately from the viewpoint of its own particular characteristics, *i.e.*, it is impossible to outline a routine treatment for chronic suppurative inflammation of the middle ear with the idea that it will be efficacious in any great number of cases. This ap-

plies to the practice of constant syringing, as well as to the adoption of the usual surgical procedures for the relief of the discharge. From the fact that a discharging ear must always be considered dangerous to the health or even the life of the individual, the rule prevails that if a given case fails to yield to non-surgical treatment, more especially in the presence of extensive attic caries or cholesteatomatous masses, surgical intervention is called for. To be conservative, the first procedure should be the **removal of all inflammatory débris** and an **ossicectomy**, provided the symptoms do not de-

nitrate, to the ounce (30 c.c.) of water. These solutions are to be *warmed* and dropped into the ear after it has been thoroughly cleansed by syringing and then dried. They are used to the best advantage by placing the head on a table, with the affected ear uppermost; the canal is then to be filled with the medicinal solution, which is allowed to remain about five minutes. When the attic is especially involved the solutions can be used to advantage by means of the **tympanic syringe** (Fig. 7).

Except for the use of the tympanic syringe, this treatment can usually be carried out at home, from 1 to 3



Fig. 7.—Tympanic syringe.

mand a radical mastoid operation. Ossicectomy failing to effect a cure, a **mastoid operation**, usually of the radical type, is indicated.

Whatever the line of treatment, the object is to bring about a cessation of the discharge, and this is accomplished, in the average case, where the discharge is profuse, by first **syringing** the ear, to rid the canal and tympanic cavity of secretion, and then drying it.

Following this, in some cases, the insufflation of **boric acid powder** or a combination of **boric acid** and **zinc oxide powder** in equal parts will act very satisfactorily. It will be necessary, at times, to use astringent solutions, *e.g.*, from 5 to 8 grains (0.3 to 0.5 Gm.) of **zinc sulphate**, **copper sulphate**, or **lead acetate**, or 10 to 20 grains (0.6 to 1.2 Gm.) of **silver**

times a day, according to the severity of the case.

If granulation tissue or non-fibrous polypoid growths be present, they can usually be eradicated by the use of **alcohol drops** in the manner described above. It is well, in the average case, on account of the pain caused by pure alcohol, to dilute it one-half with **boroglyceride** or plain **glycerin**. As the solution is used, the bottle containing it may be kept filled with alcohol, which will gradually replace the glycerin, until finally pure alcohol is used.

When the perforation is small and the discharge continuous, it is necessary to enlarge the former to provide for better drainage and to insure that the solutions and applications shall come into direct contact with the inflamed mucosal lining of the middle

ear. It must be remembered that frequent syringing is apt to keep up the discharge in some cases, in which event it is better to resort to the so-called "dry" treatment. This, as above stated, is applicable to those cases where the discharge is not too profuse, and consists of wiping out the external auditory canal, and middle-ear cavity if the opening in the drumhead is sufficiently large, with cotton on a cotton-carrier, and then applying one of the astringent solutions above mentioned, after which the entire surface is dusted with **boric acid powder** or equal parts of **boric acid** and **zinc oxide** powder, or **aristol**, plain or in combination with **boric acid**. All solutions and drops should be sterile so far as possible, and should be warmed before use. The following solutions are ordinarily used for syringing and irrigating the ear: **Saturated boric acid solution**, **normal salt solution**, 1 per cent. **lysol solution**, and 1:5000 or 1:10,000 solution of **potassium permanganate**.

The use of **autogenous** or **stock vaccines** has come into vogue in recent years, with more or less reported success. My personal experience has been decidedly disappointing, but it is well, in some instances at least, to employ this therapeutic measure. Various **caustics** and the **galvano-cautery** are at times used for the destruction of granulation tissue and polypoid growths, but as a general thing it is better to remove these by surgical means. If this, in connection with the above-mentioned non-surgical treatment, does not cure suppurative otitis media, then one must seriously consider the advisability of more extensive surgical intervention. The first step in this, in the absence

of urgent symptoms, is an **ossiculotomy**, to be followed later, should it fail to effect a cure, by a radical **mastoid operation**.

CHRONIC CATARRHAL OTITIS MEDIA (Otitis Media Chronica Catarrhalis).

DEFINITION.—A chronic catarrhal inflammation of the middle ear.

SYMPTOMS.—There are three principal symptoms of this disease: The first is a slowly progressive deafness, unrecognizable, in some instances, until the hearing in one ear is greatly impaired. Noises in the head, except in otosclerosis, are secondary to the impairment in hearing, and yet, on account of the slow progress of the latter, tinnitus aurium is frequently the first symptom of which the patient complains, and he is surprised when informed of his loss of hearing. When the second ear becomes involved, progress is frequently very rapid, the patient in such circumstances quickly losing much hearing. Attacks of dizziness and vertigo are later manifestations, and often are indicative of internal ear involvement. The symptoms are usually aggravated in damp weather.

Nearly every case gives a history of frequent "colds in the head," at which times the symptoms are increased. On relief from the coryza, the deafness and noises gradually subside and for the time being may even seem to disappear. It is doubtful, however, whether the ear ever entirely recovers itself following these attacks. The rule is that each attack adds somewhat to the progressive loss of hearing. Fatigue, mental troubles, and impaired health adversely affect the hearing. Unless the internal ear becomes secondarily

involved, complete deafness never occurs.

Notwithstanding that deafness is inconvenient and annoying, yet it is nothing compared to the distressing symptom of tinnitus aurium. The noises may be of any type, the more common being the hissing of steam, buzzing sounds, hammering, and those of a pulsating character. They are usually intermittent at first, later becoming constant, and frequently disturbing the patient's slumber. In extreme instances patients court death rather than endure this incessant torture.

The attacks of vertigo vary from slight giddiness, almost unrecognizable, to ones of such severity that the patient suddenly falls. These attacks occur in the later stages of the disease. When the stapes becomes firmly fixed in the fenestra ovalis, nausea and vomiting, together with a marked increase in the deafness and tinnitus, frequently develop. These attacks, known as *Ménière's symptom-complex*, closely simulate true Ménière's disease.

Actual pain is sometimes experienced on hearing loud noises, a condition known as *hyperesthesia acoustica*. A symptom considered unfavorable is known as *paracusis Willisiana*, or hearing better in a noise; this occurs in late stages of chronic catarrhal otitis media or otosclerosis.

The membrana tympani is usually thickened and retracted, the latter condition being due to obstruction of the Eustachian tube and the former to inflammatory changes. The drum-head may be uniformly opaque or its opacity may appear in patches. Chalky and calcareous deposits are sometimes seen. In the atrophic type

of case the membrana tympani, as well as the mucous membrane of the tympanic cavity and tube, becomes very thin. If the patient suffers from a hypertrophic nasopharyngitis or an atrophic nasopharyngitis, the same condition is very apt to be reflected in the organ of hearing.

In uncomplicated middle-ear catarrh tuning forks of high pitch are well heard, bone conduction is good, and Rinne's test is either partially or wholly negative. As the internal ear becomes involved, there is a gradual loss of bone conduction and perception of high-pitched notes.

ETIOLOGY.—This disease, in so far as we are able to determine, is the result of repeated attacks of the acute or subacute varieties. The onset is usually so gradual that often the patient is not aware of any aural abnormality until he suddenly discovers the unmistakable symptoms of well-advanced catarrhal otitis media, such as a loss of hearing or the advent of tinnitus aurium in one or both ears. Ordinarily the two ears are not simultaneously involved to the same extent. In such cases it is most difficult to assign an actual cause for the condition. As is the case in most other ear diseases, this is unquestionably an extension of a similar disease from the nasopharynx; consequently, any abnormality of this region, especially in the form of a more or less continuous congestion, must be considered as a predisposing cause. This congestive state is largely enhanced by the excessive use of tobacco (more especially cigarettes) and alcohol, obstructed nasal respiration, a dusty atmosphere, and unhealthful surroundings. Systemic diseases, such as syphilis, Bright's

disease, rheumatism, and gout, are also predisposing factors.

It is doubtful whether heredity plays an important part in the causation of chronic catarrhal otitis media, unless to this cause can be attributed that variety known as *otosclerosis*, or inflammation of the labyrinthine capsule. Hereditary *otosclerosis* does seem actually to exist in families and connections where the ancestors for several generations have been afflicted with gout. Chronic catarrhal otitis media is essentially a disease of adult life.

PATHOLOGY.—When catarrh persists, the mucous membrane re-

PROGNOSIS.—Very much depends on the patient's general health, as well as the changes that have taken place in the tympanic cavity and labyrinth, at the time he seeks treatment. Unquestionably the average case is amenable to treatment if seen in the early stage, *i.e.*, before the changes above mentioned have taken place; whereas in advanced cases all that one can hope to accomplish is the alleviation of symptoms and the arrest of the disease. In extreme cases one is often unable to effect any betterment; indeed, these cases usually go from bad to worse regardless of what may be done for them.

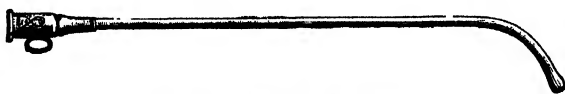


Fig. 8.—Eustachian catheter.

mains swollen from round-celled infiltration. The hypertrophic mucosal lining filling the niches of the round and oval windows binds down the ossicles, greatly interfering with their mobility, and thereby causing much impairment of hearing. In the absence of resolution, histological changes transform this hypertrophic tissue into new connective tissue, with resultant adhesions between the ossicles and the inner wall of the tympanic cavity.

In the same manner a stricture of the Eustachian tube may develop, while, on the other hand, atrophy of the tympanic mucosal lining and of the membrana tympani may take place.

What was formerly known as "chronic dry catarrh" is now recognized as a disease of the labyrinthine capsule, *otosclerosis*, a condition still much discussed.

TREATMENT.—As in other forms of aural disease, every effort must be made to **remove the cause**, which commonly resides in the nasopharynx. By the time the usual patient seeks relief, gross pathological changes which necessarily prevent a complete restoration to the normal have already occurred. One's efforts, then, must be directed to the alleviation of symptoms and the arrest of the process. Undoubtedly certain cases are made worse by meddling treatment.

Therapeutic measures should consist of the application of **local treatment** to the ears, of the **correction of nasopharyngeal disease**, and of efforts toward the **betterment of the patient's bodily health**. Inflation of the **tympanic cavity** through the Eustachian tube is carried out either by Politzer's method or the use of the Eustachian catheter. (Fig. 8.) It is well to determine in advance

whether the individual case is of the *atrophic* or *hypertrophic* variety. In the latter instance some difficulty may be experienced in rendering the tubes patulous; in the former much damage is frequently done by using undue force in a tube already abnormally patulous because of atrophic changes, the injury being either to the membrana tympani or to the labyrinth. A few drops of **chloroform** in the bag will facilitate tympanic inflation.

If the membrana tympani is firmly adherent to the tympanic cavity no

under these circumstances it should be continued, provided it does not actually impair the hearing power.

Medicated vapors and fluids, introduced by bag and catheter through the Eustachian tube, are commonly used. I have great doubt, however, as to their actual efficiency. The probabilities are that the chief benefit derived is from the act of inflation itself, rather than directly from the vapor or fluid. Alexander Randall reports good results from injecting a solution of **dionin**, 5 to 8 grains (0.3 to 0.5 Gm.) to the ounce, through the

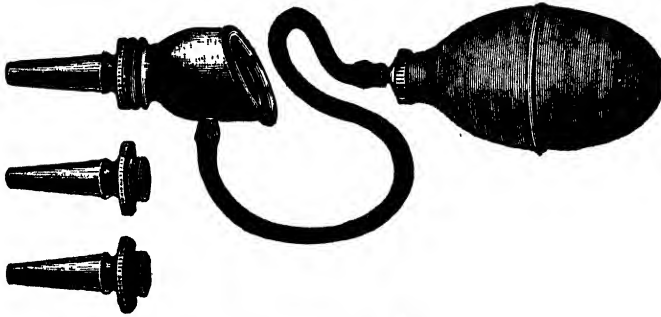


Fig. 9.—Siegle's otoscope.

improvement will follow inflation. If it is not adherent, on the other hand, even though it be in actual contact, much improvement frequently follows inflation. If no improvement is noted after inflation when the treatment has extended over several days, the case is not a very hopeful one, and this particular line of treatment should be less frequently used or altogether abandoned. Should inflation by Politzer's method or the use of the Eustachian catheter result in improvement, the same measure should be employed about twice a week as long as the benefit continues. In some instances inflation will be beneficial to the tinnitus even though it does not improve the hearing, and

catheter and Eustachian tube into the middle ear. **Liquid petrolatum** and **zinc oleate** are also used, in the same manner. A 2 per cent. solution of **pilocarpine**, as first suggested by Politzer, is still a favorite medication, especially when syphilitic involvement is suspected or actually present. A 10 per cent. aqueous solution of **potassium iodide** is used in similar cases. All solutions and instruments, and the nasopharynx so far as possible, should be thoroughly sterile. It must be remembered, also, that even though solutions be sterile, they are apt to induce an acute middle-ear inflammation if too large a quantity is used, 2 or 3 drops being sufficient. Three or four days

should elapse between treatments of this type.

Bougies are used to determine the existence and location of a stricture, as well as to dilate it, and to apply local therapeutics if a medicated bougie is employed. They are resorted to when other methods fail to render the tubes patulous, and should be used only by experts.

Treatment by way of the Eustachian tube may be supplemented by **vibratory massage** through the external auditory canal. For this purpose Siegle's otoscope (Fig. 9) or other similar appliances, some of which are run by electricity, are of undoubted value, more especially in the hypertrophic form of the disease. In using Siegle's otoscope, great care must be taken that the bulb is compressed before the aural tip is introduced into the meatus, as otherwise the effect would be to push an already retracted drumhead and impacted stapes into still more abnormal positions. These aural gymnastics are indicated in all hypertrophic cases except where the malleus is adherent to the promontory. In such cases the effect would be to relax still further the membrane on each side. Generally speaking, aural massage is contraindicated in the atrophic variety of cases.

If dizziness and vertigo persist and become extreme, the labyrinth is usually seriously involved.

Dividing the adhesions that bind down the drumhead and ossicles to the promontory offers a means of improvement in those well-advanced cases where ossicular ankylosis is not complete and the labyrinth is not unduly involved.

Various operations on the mem-

brana tympani and partial or complete **extraction of the ossicles** have been suggested and frequently performed in the past, without sufficiently permanent results to warrant serious consideration except in extreme cases in which other therapeutic measures have failed to give relief.

Improvement of the general health, by whatever means will promote its betterment, should be given careful consideration. The internal administration of **compound wine of iodine**, which contains $\frac{1}{6}$ grain (0.01 Gm.) each of iodine and bromine and $\frac{1}{100}$ grain (0.0006 Gm.) of phosphorus to the dram (4 c.c.), has given very satisfactory results. This remedy, to be efficient, should be continued over a long period of time, and has the advantage of acting as an alterative tonic without in any degree interfering with the patient's digestive apparatus. The administration of full therapeutic doses of **strychnine**, alone or in combination with the **glycerophosphates**, is of value. **Syrup of iodide of iron** is frequently prescribed. **Ergot**, in rather full doses, is sometimes beneficial for the relief of tinnitus aurium, more especially the pulsating type.

Derangements of the thyroid gland are unquestionably responsible for some cases of impaired hearing accompanied by tinnitus aurium. These cases will not only improve, but, as a rule, entirely recover, upon administration of appropriate doses of **thyroid extract**. The patient should lead as much of an **out-of-door life** as possible, and take moderate **exercise**. Those living in low regions, with a moist atmosphere, will frequently be benefited by going to a **greater alti-**

tude, with clear atmosphere; while the reverse is true of those living in great altitudes.

ACUTE MASTOIDITIS.

SYMPTOMS.—These typically comprise severe pain in the mastoid region, tenderness, fever, and swelling of the auditory meatus above and posteriorly. A deep boring pain extending to the region behind the ear is more suggestive than a lancinating, intermittent pain. A sagging tendency of the postero-superior part of the drum, coupled with profuse discharge from the middle ear, is almost diagnostic even in the absence of other symptoms. All these evidences point to actual retention of pus in the mastoid; where there is no hindrance to the exit of pus they need not necessarily appear.

In subacute cases many of the symptoms may have shown a tendency to subside, but tenderness persists for a few weeks or months, after which an acute condition abruptly returns, calling for immediate operation. There occur also cases of latent mastoiditis, where even tenderness and discharge may have subsided, but acute trouble later returns. Cubet-Barbon suspects latent mastoiditis where, after the drum has been freely opened, thoroughly washed through the meatus, and its fundus carefully dried, a droplet of pus at once reappears at the opening.

In children mastoiditis is more regularly acute than in adults, and a subperiosteal abscess may be formed within a short time.

Where a discharge from the meatus in acute otitis suddenly stops and remains in abeyance for more than a few days, mastoiditis requiring operation is likely to develop. In the most acute cases of mastoiditis, usually streptococcic, only a few days may separate the initial symptoms and the moment at which surgical evacuation of the mastoid becomes indicated. In other cases slight tenderness on deep pressure and mild shooting pains through the mastoid may persist for weeks, and operation remain unnecessary, a fluctuating swelling finally appearing over the mastoid or the digastric fossa, or more deeply in the neck tissues, the result of perforation of the bone and passage of pus into the soft tissues.

ETIOLOGY.—Tuberculosis, syphilis, or trauma of the mastoid may induce an apparently primary mastoiditis, in which, if caries of the bone occurs, the abscess cavity is generally not connected with the tympanum. Almost always, however, mastoiditis in any of its forms is a consequence of pre-existing acute or chronic suppuration of the middle ear.

DIAGNOSIS.—A pushing out of the auricle from the head, when viewed from behind, is deemed significant of mastoiditis, enlargement of the small lymph node over the surface of the mastoid not causing this condition. A bacteriologic examination of the discharge should be made, as the type of organism found governs the urgency of operative treatment.

The X-rays are of diagnostic value, serve to show the size and extent of the mastoid cells in the individual case, and assist in convincing the patient of the necessity of an operation where indicated.

No clinician should depend entirely on the X-ray evidence, especially in deciding upon operation, though in the author's series the X-ray failed to show disease only in 2 cases. Both mastoids should always be studied, but it must also be remembered that Dixon found, in a study of 522 cases, asymmetrical mastoids in 14.5 per cent. It is the variation in type—i.e., whether a mastoid is pneumatic, undeveloped, diploetic, or sclerotic—that makes interpretation difficult. G. E. Pfahler (Ann. of Otol., Rhinol. and Laryng., Sept., 1924).

PROGNOSIS.—Recovery without operation, the patient having sufficient resistance to permit of complete drainage through the aperture in the tympanic membrane, is uncommon. In cases operated on within the first 4 or 5 days the operative mortality, under proper conditions, is less than 1 per cent. In cases infected with *Streptococcus mucosus capsulatus* earlier operation is needful and the prognosis is less favorable than in staphylococcic infection.

Unoperated cases are exposed to grave complications such as lateral sinus phlebitis, thrombosis, and embolism. Subdural abscess, meningitis, brain abscess, and septicemia are also possible complications.

TREATMENT.—In beginning acute mastoiditis, pain may be combatted with the **ice-bag**, to be replaced in 36 hours by a **hot water bag** if the cold has failed to relieve the pain considerably and promote escape of secretions. An analgesic drug may be administered, and **morphine** hypodermically once or twice is permissible provided not enough is given to obscure the symptoms. Some recommend **leeching**. The ear should be **irrigated** frequently with an antiseptic, such as hot **boric acid** solution, and **active bowel movements** secured. **Shrapnell's membrane** should be **incised** when its posterior part and the surrounding meatal tissues are found congested. Leland has recommended an "abortive treatment" consisting of **multiple incisions** in the drum-head and the introduction of warm **Wright's solution** and a light **gauze wick**, covered with a **dry pad**—to be changed when wet.

Operative treatment is indicated where the above measures, coupled with proper management of middle ear suppuration, fail to give relief. According to D. M. Griffith, if discomfort and discharge are not lessened in 5 to 7 days, and all symptoms persist, operation is imperative. Where some doubt as to its necessity exists, it seems wise to incline toward the intervention, both the danger to life and that of loss of hearing being greatly reduced by it.

The customary operative procedure is the **simple mastoid** or **Schwartz operation**. The incision, crescentic in shape, is made from the tip of the mastoid to a point above the helix, and passes rather close to the auricular attachment. It is continued upward almost to the temporal artery, and should penetrate to the bone, the periosteum being cut through. The lips of the wound may be held apart with Jansen dilators above and below, after the periosteum has been carefully raised for some distance. The cortex of the mastoid, if softened, is then rather easily removed with bone forceps or curette, and any abscess cavity found scraped clean down to normal bone with the curette, special care being taken at the points where the lateral sinus and aqueduct of Fallopius might be injured. The mastoid antrum should then be thoroughly opened up and the bone above and behind the meatus chiselled away to obviate sinus formation from cells overlooked in this

locality. In cases of *von Bezold's abscess* (an abscess below the mastoid process, extending down into the tissues of the neck), due to perforation toward the midline on the inner surface of the mastoid process, the whole tip of the mastoid should be removed and the underlying abscess cavity well opened up. In cases in which the mastoid, upon exposure, shows no area of softening or sinus opening, entrance into the mastoid is effected with a chisel and mallet, in a safety space called the triangle of Macewen or suprameatal triangle, bounded in front by the posterior wall of the meatus, above by the linea temporalis, and behind by the remains of the squamomastoid fissure. The antrum will be penetrated at a depth of 12 to 22 millimeters from the surface, the operator proceeding with great caution in the latter part of this distance. Upon working in a direction slightly upward and parallel to the auditory canal, a right-angled probe, passed into the vault of the tympanum through the meatus, will eventually be encountered, with relative safety. The wound is then thoroughly washed out with very hot saline solution, and usually, a primary suture effected, with a small piece of packing starting from the antrum and emerging at the lower end of the wound. In cases with deep complications, however, the whole wound is lightly packed with iodoform or bismuth gauze.

CHRONIC MASTOIDITIS.

SYMPTOMS.—Except in a few traumatic cases, chronic mastoiditis is always preceded by middle ear suppuration, and the symptoms produced are similar. At times there is little or no pain. The condition may not be suspected until examination reveals congestion of Shrapnell's membrane, associated with postero-superior swelling in the meatus. Enlargement over the mastoid or of the tissues below the ear may, however, suggest its presence from the exterior. Where perforation has occurred, the typical pushed-out appearance of the auricle will be noted on posterior inspection.

PATHOLOGY.—Usually the mastoid antrum is occupied by cholesteatomatous masses, *i.e.*, accumulations of epithelial scales, dried pus, and cholesterol crystals. These masses are apt to shut off the mastoid cells from the tympanic cavity. Almost

complete obliteration of the cells may also result from thickening of the tissues adjoining a carious portion of the bone. Where no suppuration has occurred in the preceding active inflammation, consolidation of the mastoid by hyperostosis may be induced in the absence of bone caries.

TREATMENT.—The initial measures indicated are those calculated to clear up the underlying chronic suppurative otitis media, including at times such minor operative procedures as **removal of aural polypi, ossiculectomy, and closure of the Eustachian tube (Yankauer operation).**

Where such conservative measures fail to arrest the discharge or the odor, more thorough surgical intervention is indicated. The **simple mastoid operation** should prove sufficient where the disease is limited to the antrum and mastoid cells. In many instances, however, it fails to eliminate and cure the condition completely. In 1891 Stacke introduced the **radical mastoid (Schwartz-Stacke) operation**, which aims to remove all diseased bone from the middle ear, attic, antrum and mastoid, throwing these spaces, along with the auditory canal, into a single cavity. The antrum is first opened as in the simple mastoid operation, and the cartilaginous portion of the canal with the periosteum separated from the bony canal by elevation, incision, and traction. The mastoid antrum and cells are usually next excavated as in the simple mastoid operation. The bony canal is now chiselled off down to the annulus tympanicus, care being taken not to endanger the facial nerve. The bony external wall of the attic and aditus is then gouged and curetted off, the tendon of the stapedius muscle and the incudostapedial articulation severed, and removal of the malleus and incus effected. The external walls of the antrum, attic, and hypotympanic space are next curetted away to eliminate projecting bony margins and round out the cavity as a whole. Finally, oozing is checked, and as much as practicable of the cavity remaining lined with flaps of skin from the meatus and the concha. The uncovered area is permitted to heal by granulation or grafted at the operation or later with Thiersch grafts. The cavity is packed, the end or ends of the packing being brought out of the ear canal. Behind the auricle the

periosteum is first sutured, then the subcutaneous tissues and skin. Finally, a sterile mastoid dressing is applied. Unfortunately, improvement in hearing from the radical operation cannot be promised.

S. MACCUE SMITH,
Philadelphia.

MIGRAINE. See NERVES, PERIPHERAL, DISEASES OF.

MILIARIA (PRICKLY HEAT).

—**DEFINITION.**—Miliaria (prickly heat; lichen tropicus; miliaria rubra; miliaria alba) is a vesicular eruption of the skin characterized by discrete, but closely set, pinpoint- to pinhead- sized papules and vesicles occurring at the mouth of the sweat-ducts, accompanied by itching and burning, and due to profuse sweating.

SYMPTOMS.—The eruption of miliaria consists of minute vesicles developed near the pores of the skin. These may be acuminate and red (lichen tropicus) and discrete and irregularly dispersed over the surface; or, they may be confluent and red at the base (red miliaria). At first they contain a pellucid fluid, which occasionally tends to become turbid, then purulent. The eruption is apt to be present in parts of the body covered by clothing. The vesicles usually dry up into minute scales. Sometimes the case is attended by lesions simulating those of eczema.

The active symptoms generally consist of a prickling sensation as if thousands of needles were being forced into the skin. This is followed by pruritus, and the case then proceeds to recovery if the irritating factor (heat) is avoided.

DIAGNOSIS.—Miliaria is distinguished from eczema by the sudden, profuse occurrence of the eruption following sweating, by the discreteness and non-coalescence of the lesions, by the absence of weeping, and by the spontaneous cure on the appearance of cooler weather.

ETIOLOGY AND PATHOLOGY.—The immediate causes of miliaria are excessive stimulation of the sweat-glands and unusual activity of function, brought on by exercise during the summer, or exposure to severe heat. In tropical climates it may occur at any time during the year, but in the temperate zone it is

met with only during warm weather. Too heavy or too light clothing may aid in its development. Children and the obese are more liable to attacks of the papular variety; also persons of nervous temperament and fair complexion. Weak and anemic persons—pale, overworked women; puny, ill-fed infants, and young children—are more subject to the vesicular form.

The condition has been ascribed by Pearse to obstruction of the sebaceous glands; by Robinson, to inflammation about the sweat pores; by Török and Castellani, to irritation by the sweat. Milian emphasizes abnormal composition of the sweat in the causation of red miliaria.

Histologically, Politzer found an edematous rete Malpighii, with dilated sweat-ducts, and the horny layer of the epidermis swelled by imbibition.

TREATMENT.—The treatment is mainly prophylactic: measures calculated to reduce undue exposure of the body to heat. When unavoidable climatic conditions act as cause, frequently repeated **bran baths** (a pound of bran packed in a towel being allowed to soak) are sometimes very soothing. A solution of **ammonia**, a tablespoonful to a quart of water, generally allays the itching very promptly. Sponging with **lime water** is preferable in children.

Pearse advises the use of a mixture of **sweet almond oil** and **lanolin** (8 to 1), the parts being anointed night and morning, with gentle massage. As the excessive sweating is liable to cause eczema intertrigo, **drying powders** for the axillæ, under large mammae, and between the skin folds of fat people are useful.

In the graver form Holstein states that **thorough cleanliness** must be insisted upon; the clothing should be boiled, and **sublimite washes** or **ointments** employed. In some cases the crusts of the lesions may be removed and **hydrogen dioxide** applied. This should be repeated daily for several days, antiseptic ointments being applied between-times.

Phenol, **menthol**, **aristol**, **euophen**, **resorcinol**, etc., and lotions of **ichthyol** (2 to 5 per cent.) made with a saturated solution of **boric acid** have been recommended by other authors.

W.

MILIARY FEVER (SWEATING SICKNESS).—DEFINITION.

—An infectious disease characterized by an acute inflammation of the sweat-glands, accompanied by the appearance of small vesicles, much burning, itching, pains, fever, and chills, and extraordinarily profuse sweats, usually affecting adults between the ages of 20 and 40. Vignol reported an epidemic of 6256 cases, with a mortality of 2 per cent. Weichselbaum reported 3 epidemics, with mortalities of from 16 to 32.3 per cent.

SYMPTOMS.—These are fever, with its usual phenomena, irritation of the skin, epigastric oppression, profuse and persistent sweating, followed, on the third or fourth day, by an eruption of miliarial vesicles accompanied by much burning, itching, and pain. The vesicles burst, and within 48 hours the disease is terminated by a scaly desquamation. In severe types grave nervous phenomena (delirium, etc.) are present, hemorrhages may occur, and fatal collapse may ensue. Relapses are not uncommon.

ETIOLOGY AND PATHOLOGY.—

Chantemesse advanced the hypothesis that field rats are responsible for the transmission of the disease, on the ground that it is never observed in cities; that direct contagion does not occur; that the regions affected in the large epidemics were exclusively those ravaged by field rats during the previous few years, and that the victims all showed flea bites, ascribing unprecedented swarms of fleas to the invasion of their homes by the rodents. Most epidemics occur in spring and summer. The disease is more common among women than men, and is most frequent in middle life.

According to Weichselbaum the sudamina, whether nodular or vesicular, are never caused by retention of fluids in the sweat-glands, but are always of an inflammatory nature, as shown by serial sections. The lesions are found, principally, in the epidermis, though some changes are present in the corium. The disease does not appear to be contagious.

PROGNOSIS.—This varies with the character of the epidemic, the average mortality apparently being 8 or 9 per cent., though it may reach as high as 32.3.

TREATMENT.—There is no prophylactic measure save **disinfection**. There is no specific treatment. The sweating may demand **atropine** for its control. **Sedative** remedies may be employed to overcome the marked nervousness frequently noted at the beginning of the disease. **Quinine** has been generally used to control the fever. The expectant plan of treatment has found most favor. **Calomel** in small doses, when administered early, is believed to shorten the disease. Lukewarm **bran baths** or **sponging with lime water** assist in allaying the itching and encourage resolution. The **body covering** should be **changed as often** as it becomes soaked with perspiration. The **diet and bowel functions** should be **regulated** as in other acute fevers. W.

MILIUM.—Miliun (grutum; strophulus albidus) is a cutaneous disorder characterized by the formation of small, roundish, whitish or pearly, sebaceous, non-inflammatory elevations, situated just beneath the epidermis, which are formed by the accumulation of inspissated sebum in ducts the outlets of which have become occluded. They are mainly found on the face, eyelids, and foreheads of elderly persons, may exist in large numbers, and vary in size from a pinhead to a small pea. They may undergo calcareous degeneration, forming cutaneous calculi.

According to Pusey, milium is most frequently the result of the growth of the horny epidermis over the mouth of the sebaceous follicle. The lesions differ from comedones only in that the contents of the distended duct cannot be squeezed out until an opening is made. Milium is often associated with comedo and acne. When present in infants milium usually disappears spontaneously after a time, but not in adults.

TREATMENT.—Through a small **incision** over the elevation the contents may be expressed by squeezing. The interior should then receive an application of **silver nitrate** (solid stick) or of **tincture of iodine**. **Electrolysis** may also be resorted to. Where the milia are numerous and close together the use of a **peeling paste** or **soft soap** long enough to bring on a mild dermatitis will often result in their exfoliation. In children

extra care as to the cleansing of the skin and the use of a weak **sulphur ointment** are likely to prove effectual. S.

MILK SICKNESS.—This is a disease of cattle (the "trembles," "slows," "alkali poisoning"), but is occasionally observed in women, being communicated to them by use of the flesh or milk of animals suffering from the disease. In cattle it is due to the ingestion of various toxic plants, such as the white snakeroot, *Rhus toxicodendron*, the rayless goldenrod, etc., and is usually met with on the banks of streams. Moseley, from experiments on rabbits, concluded that the condition is due to aluminum phosphate, which in Ohio and Illinois animals get by eating white snake-root, in New Mexico by eating the rayless goldenrod. The disease is commonest in the Central and Southeastern States.

SYMPTOMS AND PATHOLOGY.—The symptoms in the main are persistent vomiting, obstinate constipation, sweetish acetone odor of the breath, thirst, swollen tongue, muscular weakness, abdominal pain, and prostration. Restlessness may pass into stupor and coma, death following. There is little or no fever. Little is known as to the incubation period. Convalescence is slow.

According to Jordan and Harris, the chief pathological lesions in cattle are parenchymatous changes in the liver, heart muscle, kidneys, and small intestine. The changes are those of a parenchymatous nature, such as are frequently produced by toxic action in general; namely, cloudy swelling and fatty metamorphosis. The severest action is shown in the liver-tissue. In the organs other than those mentioned above nothing of very particular interest could be noticed. These observers found in the tissues and body fluids of infected animals a bacillus which they termed *B. lactimorbi*, the direct connection of which with the disease is, however, unproven. Phillips claimed to have found a spirillum in the blood.

TREATMENT.—This consists in removing all possible causes and aiding the autoprotective resources of the body. Wilkinson found treatment of the acidosis with **glucose** in the form of **molasses** very helpful. Besides tonics, the use of **creosote**

They may contain sodium and calcium bicarbonates and sodium chloride and sulphate. These waters are almost all cold and of pleasant taste and are, in some cases, further charged with carbonic acid before export. They are cold waters.

Physiological Action.—The physiological action of these carbonated waters appears to be due to the effect of the gas on the nerve-ends of the mucous membrane. The carbonic acid gas escaping from the water causes an agreeable prickling sensation in the mouth and gullet, while in the stomach a sensation of warmth and slight distention are felt. This distention and stimulation cause the stomach to contract and expel the gas by the mouth. The intestines are seldom affected unless they are in an irritable condition, when slight peristalsis is induced. The effect upon the nervous system is one of freshness and exhilaration, due to the reflex excitement of the nerve-centers through the stimulation of the nerve-endings of the tongue, palate, and stomach. The absorption of aerated waters is more rapid than that of plain water, and hence produces a more rapid flow of urine. Glax holds that aerated waters raise the blood tension, a general effect of drinking cold water.

Therapeutic Uses.—The aerated waters are useful in irritable conditions of the stomach; mixed with milk or alcohol, the latter are made tolerant to the stomach. Used as table waters, they stimulate the appetite, and, by causing a better mixing of the food and more active movements of the muscular coats, aid digestion. When the stomach is dilated and its walls flabby, the use of aerated waters is contraindicated.

The aerated waters are useful as a gargle in subacute pharyngitis. In pruritus, prurigo, and hyperesthetic conditions of the skin carbonated waters are beneficial when used as baths.

Types: France: St. Galmier; Germany: Apollinaris; Czecho-Slovakia: Giesshübler; United States: White Rock (Wis.).

2 and 3. SIMPLE ALKALINE AND ALKALINE-SALINE WATERS.—The alkaline waters contain sodium bicarbonate as their chief ingredient. They are nearly all cold; Neuenahr Sprudel, how-

ever, has a temperature of 104° F. (40° C.), and the Source de l'Hôpital, at Vichy, one of 87° F. (30.8° C.). Many are used as table waters.

Physiological Action.—The physiological action of these waters resembles that of the carbonated waters, as the sodium bicarbonate on reaching the stomach combines with the free acids and liberates carbonic acid.

Therapeutic Uses.—The alkaline waters are chiefly employed in the treatment of affections of the mucous membranes of the respiratory, digestive, and urinary tracts, but are also popular in chronic gout and rheumatism.

In chronic catarrh of the pharynx, nasopharynx, and larynx the sodium bicarbonate in the waters aids in the removal of the thick and tenacious mucous secretions, enabling other remedies to be more efficaciously applied. At the springs the waters are used in the form of warm sprays. In chronic gastric catarrh 1 or 2 glasses of water, taken on an empty stomach, loosens and washes away the mucus from the walls of the stomach, and prepares that organ for the next meal. The alkaline waters are useful for washing out a dilated stomach. They are commonly used in hepatic disorders and in suspected obstruction of the bile-ducts from catarrh or calculi.

Many diseases of the urinary tract are benefited by alkaline waters: Highly acid urine, uric acid concretions in kidney or bladder, and catarrh of the bladder or urethra.

Types of alkaline waters: England: Bristol, Buxton; France: Vichy, Mont Dore; Germany: Fachingen, Obersalzbrunnen, Ems, Wildungen; United States: Saratoga Vichy, Ukiah Vichy (Cal.), St. Louis Spring (Mich.), Manitou (Col.), California Seltzer, Bladon (Ala.), Gettysburg (Pa.).

Types of alkaline-saline waters: France: Royet, Vals (Desirée Sp.); Germany: Ems, Selters; Czecho-Slovakia: Luhatschowitz; United States: Ballston Spa (N. Y.), Hathorn (Saratoga), Waconda Spring (Kan.), Americanus Well (Mich.), Borland Mineral Well (W. Va.), Dixie Spring (Tenn.), Hot Springs (Va.), Bethesda (Wis.).

III. MILD INTESTINAL STIMULANTS.

1. SODIUM CHLORIDE WATERS.—

In these waters sodium chloride is the chief ingredient, but other salts are always present (calcium and magnesium chlorides, sodium bicarbonate and sulphate). Some of these waters are warm—Wiesbaden, 155.6° F. (68.7° C.); Baden-Baden, 155° F. (68.36° C.); Bourbonnelles Bains, 138° F. (58.75° C.); Burtseheid, near Aix-la-Chapelle, 140° to 165.2° F. (60° to 74° C.); Battaglia, in Italy, 159.8° F. (71° C.). These waters are mostly used in baths.

Physiological Action.—The physiological action of these waters is not definitely known; but the facility of diffusion of sodium chloride, the aid it lends the diffusion of albumin, and its attraction for water may throw some light on that point.

Therapeutic Uses.—In chronic catarrh of the stomach and bowels, where there is muscular atony or deficient secretion of gastric juice, these waters do well. These saline waters remove the altered secretions, preventing their fermentation and decomposition and thus indirectly favor the secretion of the gastric juice. In hepatic hyperemia and cirrhosis these waters aid by depleting the portal system, and are more potent when they contain sodium sulphate. Inhalation of these waters is beneficial in catarrhal affections of the air passages where there is an irritable condition of the mucous membrane and scanty secretion.

Types: Germany: Nauheim (Friedrich-Wilhelm's Quelle), Baden-Baden, Kreuznach (Oranien Quelle), Homburg (Elizabethbrunnen), Wiesbaden; England: Harrogate, Cheltenham; France: Bourbonne-les-Bains; Switzerland: Rheinfelden; United States: Glen Springs (N. Y.), Geuda (Kan.), Eureka (Cal.), Akesion Spring (Mo.), Byron Surprise (Cal.), Clark's Red Cross Mineral Well (Mich.), St. Clair Mineral Spring (Mich.).

2. ALKALINE APERIENT WATERS.

IV. STRONG APERIENT WATERS.

—The chief ingredients of the aperient waters are sodium sulphate, chloride, and bicarbonate, the most important of which is sodium sulphate. The stronger aper-

ients contain in addition magnesium sulphate.

Physiological Action.—The physiological action of these waters is largely due to the attraction of the sodium sulphate (Glauber's salt) for water, and to the difficulty with which they pass through membranes (osmosis). Hay found that the saline purgatives increase the intestinal secretions, not by osmosis, but by the irritant and specific qualities of the salt, and also probably by its bitterness. By reason of the low diffusibility of the salt, the fluid secreted into the intestine it not readily absorbed; the fluid accumulates, and, causing increased peristalsis, reaches the rectum, where it gives rise to purgation (Huggard). After some hours the salt causes diuresis, and with it a secondary concentration of the blood, which continues during the activity of the diuresis. An increased blood-pressure follows the ingestion of these waters.

Therapeutic Uses.—These waters are largely used in obesity, gastric and intestinal catarrhs, liver affections, gallstones, pelvic congestions, and old exudates. Gout, rheumatism, and arthritic affections are benefited when special indications are present, in robust subjects, for action upon the alimentary canal. The continued use of these waters causes irritation of the mucous membrane of the bowels. The duration of the "cure" with these waters is usually twenty-one days (Huggard).

Types: Czecho-Slovakia: Marienbad, Carlsbad, Pullna, Seidlitz; Hungary: Apenta, Aesculap, Franz-Josef quelle, Hunyadi János; Spain: Carabaña, Rubinat; Germany: Friedrichshall, Kissingen; Switzerland: Birnmensdorf, Tarasp; United States: Clark's Riverside Spring (Mich.), Castalian Springs (Cal.), Blue Lick (Mo.), Crab Orchard (Ky.), Gibson Mineral Well (Tex.), French Lick Pluto (Ind.), Abilena (Kansas), Harrodsburg (Ky.), Bedford (Pa.).

B. TONIC AND RECONSTITUENT.

I. HEMATOGENIC.

1. IRON WATERS.—The chief constituent of these waters is iron, which may be present in the form of the carbonate or the sulphate. The carbonate of iron waters are the more numerous and important, and usually contain free carbonic acid, which

covers the styptic taste of the iron and renders them more acceptable to the stomach. The sulphate of iron waters, as a rule, contain more iron, and some contain arsenic in appreciable amounts, Roncegno (Tyrol) water having $2\frac{1}{2}$ grains (0.15 Gm.) per quart (liter).

Physiological Action.—The physiological action of these waters is that of their principal ingredient, iron.

Therapeutic Uses.—These waters are useful in anemia and in conditions dependent upon anemia. Atonic dyspepsia, chronic diarrhea, hysteria, hypochondriasis, neuralgias, and neuroses dependent upon debility or anemia are much benefited by a course of these waters, especially when aided by the pure, bracing air and pleasant surroundings at the various spas. Menstrual irregularities and uterine catarrhs are special features of the iron spas, great relief following the use of the waters.

Types: England: Brighton, Harrogate, Tunbridge Wells; Switzerland: St. Moritz (Grand Source); Belgium: Spa (Pouhon-Liège); Germany: Schwalbach (Stahlbrunnen), Homburg (Stahlbrunnen), Pyrmont (Trinkbrunnen); Bohemia: Marienbad, Franzensbad; Italy: Levico; United States: Matchless Mineral Wells (Ala.), Overall Wells No. 2 (Tex.), Brown's Wells No. 1 (Miss.), Gaylord and Gulick's Spring (Va.), Oak Orchard (N. Y.), Bath Alum (Va.), Anderson's Spring (Pa.), Rawley Springs (Va.), Cooper's Well (Miss.), Ballston Spa (N. Y.).

2. EARTHY OR LIME WATERS.—

The chief ingredient of these waters is lime in the form of the bicarbonate or the inert sulphate, and a small quantity of magnesium bicarbonate and other salts. By many authorities they have been considered harmful, while others point to the presence of lime in the tissues and secretions and assert that a certain supply is requisite to replace loss through tissue change. When lime is given for therapeutic purposes the soluble and readily absorbable preparations (chloride or acid phosphate) are preferable (Huggard).

Therapeutic Uses.—These waters have been employed in pulmonary affections (including tuberculosis and rachitis), in urinary affections (catarrh of the bladder,

kidney, and gravel), in affections of the stomach and intestines, in biliary affections, in gout, rheumatism, and diabetes, and in skin affections (chronic dry eczema and psoriasis in lymphatic or scrofulous subjects).

The administration of lime to old persons with atheromatous tendencies is considered undesirable.

Types: A. Carbonate of lime waters: France: Châtel Guyon, Pougues; Germany: Rippoldsau, Driburg, Wildungen. —B. Sulphate of lime waters: England: Bath (Somerset); France: Vittel (Vosges), Contrexéville (Vosges); Switzerland: Leuk, Baden, Weissenburg; Germany: Lippspringe.

11. ALTERATIVE AND NERVINE.

1. ARSENICAL WATERS.—These waters contain a therapeutically significant amount of arsenic, although usually named after some other constituent. Vichy water, known as an alkaline water, contains $\frac{1}{60}$ to $\frac{1}{30}$ grain (0.001 to 0.002 Gm.) of arsenic trioxide per quart (liter). The water of Bussang (Vosges), known as a simple aerated water, contains $\frac{1}{30}$ grain (0.002 Gm.) of arsenic per quart (liter). La Bourboule (France), the strongest of the alkaline arsenical waters, contains $\frac{1}{2}$ grain (0.028 Gm.) of sodium arsenite per quart (liter). Strong Levico water (Tyrol) contains $\frac{1}{4}$ grain (0.0087 Gm.) and Roncegno (Tyrol) contains $2\frac{1}{2}$ grains (0.15 Gm.) per quart (liter). The arsenical content must be borne in mind in using these waters.

Therapeutic Uses.—These waters have been employed in dyspeptic troubles due to gastric irritability, gastric catarrh, nervous indigestion and hyperacidity, and as a nerve sedative in asthma and chorea. While pharmacopeial preparations are best, these waters may be used in chronic malaria, and if an alkaline water is indicated an arsenical water may be used. The same is true in the treatment of skin diseases.

2. BARIUM CHLORIDE WATERS.—

Barium chloride exists in minute quantities in many mineral waters. The Elisabethquelle at Kreuznach contains 1 grain (0.064 Gm.) per quart (liter), the Victoriaquelle nearly $1\frac{1}{2}$ grains (0.089 Gm.) per quart (liter), and the Llangammarch Spa

TABLE SHOWING COMPARATIVE POTENCY OF REPRESENTATIVE AMERICAN AND EUROPEAN SPRINGS (JAMES K. CROOK).*

I. ALKALINE WATERS.

AMERICA.	Gm. per U. S. gal.	EUROPE.	Gm. per U. S. gal.
Saratoga Vichy	367.32	Vichy, France (Grand Grille)	311.92
Ukiah Vichy, Calif.	268.45	Fachingen, Nassau, Ger.	223.51
St. Louis Spring, Mich.	227.14	Ems (Kessel Brünnen) ..	169.75
Manistow, Colo. (Navajo)	182.23	Apollinaris, Rhenish Prus.	157.76
California Seltzer	187.15	Wellbach, Hesse, Ger.	165.27
		Wildungen, Ger. (Stadt-Brünnen)	67.44

II. ALKALINE SALINE.

AMERICA.	Gm. per U. S. gal.	EUROPE.	Gm. per U. S. gal.
Ballston Spa, N. Y. (artesian lithia) ..	1123.25	Vals, France (Desirée Sp)	535.88
Waconda Spring, Kan.	1120.65	Bourbonne (Haute Marne, Fr.)	483.47
Saratoga, N. Y., Hathorn ..	888.40	Luhatschowitz, Moravia ..	438.04
Americanus Well, Mich.	503.90	Bilin, Bohemia (Joseph's Quelle) ..	304.49
Borland Mineral Well, W. Va.	432.28	Selters, Nassau, Ger.	228.14
Dixie Spring, Tenn.	313.74	Obersalz-Brünnen, Silesia	138.08

MURIATED SALINE.

AMERICA.	Gm. per U. S. gal.	EUROPE.	Gm. per U. S. gal.
Glen Springs, N. Y. (Neptune, used for Schott-Nauheim treatment)	10503.08	Springs of Nauheim, Ger. (Friedrich- Wilhelm's Quelle)	2148.07
Geuda Springs, Kan.	1314.78	Kreuznach (Oranien Quelle) ..	1084.32
Eureka Springs, Calif.	1800.27	Homburg, Ger. (Elizabeth Brunnen)	870.96
Sweet Springs, Mo. (Akesson Sp)	1061.94	Harrogate, Eng	864.43
Lodi Artesian Well, Ind.	672.45	Cheltenham, Eng	644.00
Upper Blue Lick, Ky.	660.14	Wiesbaden, Ger. (Koch-Brünnen)	507.70

The strongest waters of this class on the globe are found in the United States. Notable examples are the Byron "Surprise" Spring of California, containing 18,773.73 grains, Clark's Red Cross Mineral Well of Michigan, 17,825.27 grains, and the St. Clair Mineral Spring of Michigan, 17,904.6 grains per U. S. gallon.

IV. SULFURIATED SALINE.

AMERICA.	Gm. per U. S. gal.	EUROPE.	Gm. per U. S. gal.
Clark's Riverside Springs, Mich.	7318.97	Carabafia, Spain	7301.23
Castalian Springs, Calif.	4422.25	Rubinat (Serre), Spain ..	5266.64
Blue Lick Springs, Mo.	610.30	Apenta, Hungary	2541.09
Crab Orchard, Ky. (Epsom Sp) ..	401.43	Püllna, Bohemia	2010.45
Gibson Mineral Well, Texas	329.65	Friedrichs-Hall, Ger.	1559.92
French Lick Springs, Ind.	371.76	Seldlitz, Bohemia	897.59

V. CHALYBEATE.

AMERICA.	Gm. per U. S. gal.	EUROPE.	Gm. per U. S. gal.
Matchless Mineral Wells, Ala.	167.91	Brighton, Eng.	14.40
Overall Wells, Tex., No. 2	144.90	Spa (Pouhon), Liège, Belgium	5.42
Brown's Wells, Miss., No. 1	36.52	Schwalbach Nassau, Ger. (Stahlbrünnen). ..	3.74
Gaylord & Gulick's Springs, Va.	31.63	Tunbridge Wells, Eng.	2.22
Oak Orchard, N. Y.	28.62	Pymont, Waldeck, Ger. (Trunk-Brünnen) ..	2.48
Bath Alum, Va.	26.78	St. Moritz (Grand Source), Switzerland ..	1.38

The figures refer to the amounts of ferruginous salts per U. S. gallon. The U. S. possesses innumerable chalybeates of the milder grades.

VI. THERMAL WATERS.

AMERICA.	Gm. per U. S. gal.	EUROPE.	Gm. per U. S. gal.
California Geysers	150°-214° F	Wiesbaden, Ger (Koch-Brünnen)	155° F.
Hunter Springs, Mont.	148°-168° F.	Baden-Baden, Ger. (Haupt-Quelle)	155° F.
Arkansas Hot Springs	76°-157° F.	Gastein, Salzburg, Austria	87°-160° F.
Glenwood Springs, Col.	124°-126° F.	Bagnères-de-Luchon, France	131° F.
Virginia Hot Springs (boiler)	108° F.	Nauheim, Ger.	98.5° F.
North Carolina Hot Springs	96°-104° F.	Wildbad, Ger.	98° F.

Some of the undeveloped thermals of the Rocky Mountain States and California issue from the earth at a boiling temperature.

* Tabulated in accordance with author's classification in "The Mineral Waters of the United States," and in Hare's "System of Practical Therapeutics."

(Wales) nearly $1\frac{1}{2}$ grains (0.09 Gm.) per quart (liter).

Therapeutic Uses. — The waters of Llangammarch have been employed in cardiac cases, but it is only fair to say that they are used in connection with carbonic acid baths of the Nauheim type and other treatment.

In concluding the consideration of mineral springs, we quote James K. Crook, of New York, who says: "Not merely in potency of a few individual springs, but in general variety of mineral ingredients and in all the elements which go to make up an attractive analysis and a useful medicinal water, we have within our own borders (United States), with the single exception of the sulphated salines (Hunyadi János, Carabafia, Apenta, Rubinat), better waters and more of them than are shown by any European work on this subject." A comparative table of European and American waters is appended.

[A commission has been appointed by the State of New York to erect at the Saratoga Springs a large bath house with administration building and power house and a central drink hall, to which will be conducted all the available drinking waters in the village proper and in the geyser district, so that the invalid and the luxurious will not be obliged to go to the source of the various springs whose waters are prescribed for them. The central drink hall, moreover, will permit of the service of drinking waters, either hot, warm, or cold, as prescribed by the physician, and will tend to obtain obedience to the physician's order to drink the water slowly while promenading about the pavilions or in the park. Some of the baths will be of low cost for those of moderate means, others sumptuous for those of means, and free baths for those unable to pay, while free service of drinking waters at their source will be maintained by the State.

There would seem to be little necessity, at the present time, for the sending of patients abroad to receive the benefits of spa treatment, especially when we consider the proximity and accessibility of our home resorts, the complete equipment for serving drinking waters, for giving the various baths, and the facilities furnished at many of our resorts for the various

methods of auxiliary treatment (Schott, Oertel, Nauheim, Carlsbad, and other forms of hydrotherapy, radium emanatoria, Zander inhalatoria, etc.). W.]

CLIMATOLOGY AND CLIMATOTHERAPY.

CLIMATOLOGY. — According to A. N. Bell, climatology comprises "the sum of the influences exerted upon the atmosphere by temperature, humidity, pressure, soil, proximity to the sea, lakes, rivers, plains, forests, mountains, light, ozone, electrical, and, doubtless, by some other conditions of which we have no knowledge" beyond observation of their effects. Hann and Humboldt define climate as comprising the whole of the meteorological phenomena characterizing the state of the atmosphere at any place, particularly as they affect our organs, or have influence on vegetable or animal life. The good effects of the most salubrious climate may be overcome and the development of disease invited by the neglect of proper sanitary measures and the violation of physiological laws. It is difficult to classify climates; the distinctions made are often relative or conventional. Hot and cold climates, dry and humid climates, inland and marine climates convey only a general idea.

CLIMATOTHERAPY. — Climatology studies the effects of climates and climatic conditions upon health. To mental or moral conditions or to psychological effects must the benefits of a change of climate in disease frequently be ascribed. To deprive semihelpless invalids of the home and creature comforts that they are accustomed to enjoy and add the effects of homesickness to those of their physical weakness and disease are unwarranted cruelties. The individual peculiarities of each locality must be considered, such as dryness or dampness of the soil, excess of sunshine or shade, the direction and character of the prevailing winds, the presence and character of forest trees and bodies of water, convenience of access, as well as comfortable hotel accommodations, pure drinking water, good milk and other food in abundance, and the sanitary conditions.

The United States, in its wide area, offers every variety of climate. At the seashore

or on islands some distance from the coast, an ocean climate may be enjoyed. Numerous popular resorts are to be found on the Appalachian or Rocky Mountain ranges.

The salubrity of the high tablelands of New Mexico and Arizona is acknowledged, while the valleys of California, between the foothills and the coast range of mountains, are noted for their beauty and health-giving powers. There are the cold climates of Maine and Minnesota and the hot ones of the Eastern Atlantic Coast in the Southern States, and a new-world Riviera exists along the gulf coast of Florida, especially about the Pinellas peninsula, as well as on the eastern Florida coast.

A helpful classification of climates is that offered by Hermann Weber, slightly modified, as follows:—

A. Marine Climates.

I. Marine Climates with High Degree of Humidity.

1. Warm and Moist Marine Climates:—

Madeira, Canary Islands, The Azores, Ceylon, Sandwich Islands, Bahamas, Bermudas, Virgin Islands, Cuba, Jamaica, Barbadoes, Society Islands, Tahiti, Tonga, Fiji Islands, Tristan d'Acunha, St. Helena, Florida, Georgia, South Carolina.

2. Cool and Moist Marine Climates:—

Island of Bute, Rothesay, Hebrides, Orkney and Shetland Islands, Faroë Islands, Iceland, Bergen, Marstrand, Auckland Islands, Falkland Islands.

II. Marine Climates with Medium Degree of Humidity.

1. Warm Marine Climates of Medium Humidity:—

Tangiers, Algiers, Cadiz, San Lucar, Gibraltar, Ajaccio, The Sanguinaires, Palermo, Riviera di Levante, Pegli, Venice, Balkan Peninsula, Corfu, Crimea, Lisbon, Vigo, Santander, Biarritz, New Zealand, Auckland, New Plymouth, Wellington, Nelson, Virginia Beach, Old Point Comfort, San Diego, Coronado Beach.

2. Cool Marine Climates of Medium Humidity:—

English and Irish Coasts, Newport, Isle of Shoals, Nantucket, Mount Desert, Fire Island.

(a) Winter resorts: Queenstown, Isle of Wight, Florida; Lakewood, N. J.; Santa Barbara, Cal.

(b) Summer resorts: North Coast of Cornwall and Devonshire, Wales, Ireland, Brest, North Coast of France, Belgium, Holland, Germany, Tasmania; Santa Barbara, Cal.; Monterey, Cal.

III. Marine Climates with Low Degree of Humidity.

The Western Riviera, Nice, Monte Carlo, Mentone, Naples, Capri, Ischia, Malta, The Balearic Islands, Smyrna, Athens, South Africa, Australia, New South Wales, Sydney, Victoria, Melbourne, The New Jersey Coast, Long Branch, Beach Haven, Atlantic City, Cape May.

B. Inland Climates.

I. Climates of Great Altitude, or Mountain Climates.

Davos-Platz, Davos-Dörfli, Davos-Frauenkirch Wiesen, St. Moritz, European Alpine Resorts, German Mountain Resorts, Northern Italy, Apennines and Maritime Alps, Peruvian Andes, South Africa, India, Mexico, Rocky Mountains, Colorado Springs, Denver, St. Paul, Asheville, Catskills, Adirondacks, Alleghenies, Cresson, Green Mountains, White Mountains, Glen Summit, Pocono, Kane, Schooley's Mountain, Pasadena, Cal., etc.

II. Climates of Low Levels.

Dry and Warm Climates: Africa, New Mexico, California.

Dry and Cold Climates: Minnesota, Canada.

Moderately Moist Climates: Rome, Pisa, Pau, New England States, Saratoga, Los Angeles, etc.

CHOICE OF CLIMATE IN DISEASE.

—Into the solution of this problem enter the psychical and physical condition of the patient, his finances, his ability to en-

dures the discomforts of travel, his personal preferences and habits, the nature of his disease, and the advantages and physiological effects of the proposed location. Patients with seriously impaired lungs, kidneys, or heart should not be sent to places of great altitude. Patients with exhausted vitality or evidently with a short time to live should not be sent to any great distance from home. Scenery or the incidents of travel do not interest a very sick patient; homesickness may prove mortal sooner than his disease. Moist or dusty climates, whether cool or warm, are not suitable for phthisical cases in the second or third stage; in them the progress of the disease is generally hastened.

Acute diseases are best treated at home. **Anemia** and **chlorosis** are benefited by open-air life, sunshine, and a temperature that does not forbid exercise. **Asthmatics** without heart complication or emphysema do well at mountain stations or on inland plateaus; if there is serious bronchial complication a dry climate is indicated; where the secretion is scanty, the pine woods near the coast are best. **Hyperesthetic rhinitis** patients need pure air, free from dust and pollen, as found at Bethlehem, White Mountains, Kane, or Nantucket. **Chronic bronchial catarrh**, with increased secretion and moderate cough, may be relieved at seashore, mountain, or inland resorts, the change of climate itself being beneficial. **Menorrhagia** is often made worse by sea climates; in early pregnancy abortion may occur at the seashore. **Climacteric disorders** are relieved by climatic change, the excitement of the change of scene, and the pleasures and incidents of travel. **Premature senility** is often delayed by a resort to warm, sunny and dry climates during the winter and a moderately elevated mountain climate in summer. **Phthisis**, according to W. H. Flint, requires dryness, equability, and purity of the atmosphere; he further states that there is reason to believe that the benefit derived from climatic treatment is often, in a great measure, due to accessory circumstances. A climate favorable to open-air life is desirable, as in New Mexico. Flint suggested that if hot weather improved the patient and cold weather made him worse,

he should go south, at least in the winter; if he is always better in cold weather, a northern resort, as Denver, Colorado Springs, St. Paul, etc., is desirable. Other specially famed lung resorts are the Adirondacks, Lakewood (N. J.), Asheville (N. C.).

Neurasthenia and **exhaustion from overwork**, **hypochondriasis**, and **hysteria** are benefited by combined balneotherapeutic and climatic treatment. Cases of **indigestion**, **dyspepsia**, and **chronic diarrhea** do best in a dry, equable climate. **Insomnia** is relieved by a sojourn at mountain or seashore resorts, but the locality must be one where there is freedom from noise and excitement. **Leukemia** is benefited by ocean voyages, long cruises in yachts, and by prolonged stay in Egypt and Algiers. In **malarial toxemia** mountainous regions afford a cure; while sea voyages are beneficial, damp localities are to be avoided on land. W.

MITRAL INCOMPETENCY.

See ENDOCARDIUM AND VALVES, DISEASES OF.

MITRAL STENOSIS. See ENDOCARDIUM AND VALVES, DISEASES OF.

MOLLUSCUM CONTAGIOSUM.—**DEFINITION.**—This affection, known also as molluscum epitheliale and molluscum sebaceum, is characterized by the formation of sessile or pedunculated, smooth, semiglobular tumors varying in size from a pinhead to a marble.

SYMPTOMS.—The lesions are discrete, yellowish white or pinkish in color, rounded or acuminate, imbedded within or projecting beyond the surface of the skin, and have usually a dark-colored point at the apex, from which, on pressure, can be expressed a milky, curd-like, or cheesy substance. At first the lesions are quite firm, but they soften with age. After persisting for several weeks, they slough and disintegrate, or undergo slow absorption. The tumors give rise to no pain, are always discrete, may be single or multiple, and occur usually in children or young adults upon the eyelids, face, neck, breast, and genitals. This dis-

case frequently affects several members of the same household, asylum, or school.

DIAGNOSIS.—The color, the wax-like appearance, the umbilication, and the central aperture are the diagnostic features. From molluscum fibrosum it is distinguished by the absence of the central black opening in the latter and the more general distribution.

ETIOLOGY AND PATHOLOGY.—

The disease is probably contagious, though under ordinary circumstances feebly so, and it is said to be due to a parasitic protozoön of the coccidium type.

Various authors claim to have discovered protozoa within the cells of the tumors. Herzog finds, however, that these peculiar structures are solely due to hyaline degeneration, and by a special stain he could accurately study the evolution of the so-called "molluscum bodies" from the normal basal epithelium. An interesting discovery which may explain the infectious nature of the disease is the finding of large numbers of staphylococci in the excretory ducts and the surrounding tissues.

In cases in which the central pore or depression was obvious Kreibach has found spirochetes of the *refringens* type. His observations were confined to genital cases, and he believes the infection to be a secondary one, as they were not found in those lesions in which a central depression had not developed.

PROGNOSIS.—The prognosis is favorable, though the disease may persist for months or even years. It yields readily to treatment.

TREATMENT.—Thorough inunctions with **white precipitate** or **sulphur ointment** (20 to 40 grains to the ounce) are efficacious in some instances; when they are not, each tumor should be **incised**, its contents removed, and the remaining cavity cauterized with **silver nitrate**, **phenol**, or **tincture of iodine**. Raven has used **sodium ethylate** in an extensive case of molluscum contagiosum. A single application sufficed to remove most of the tumors. Pedunculated lesions may be removed with scissors, silver nitrate being then applied to their bases. General tonics (**iron**, **arsenic**, and **strychnine**) are often indicated.

W.

MONOBROMATED CAMPHOR. See CAMPHOR.

MORBILLI. See MEASLES.

MORPHEA. See SCLERODERMA.

MORPHINE AND MORPHINISM. See OPIUM.

MORVAN'S DISEASE. See SPINAL CORD, DISEASES OF.

MOUNTAIN ANEMIA. See PARASITES, DISEASES DUE TO.

MOUNTAIN FEVER. See MALARIAL FEVER.

MOUNTAIN SICKNESS. See RAREFIED AIR, DISEASES DUE TO.

MOUTH, LIPS, AND JAWS, DISEASES OF THE.

CATARRHAL STOMATITIS.

DEFINITION.—An acute inflammation of the mucous membrane of the mouth, usually caused by local irritation or occurring in the course of exanthematous diseases or prolonged febrile disorders.

SYMPTOMS.—Although the entire buccal membrane may be involved,—that of the tongue, lips, and cheeks,—the labiogingival region is usually the seat of the most active inflammatory manifestations. Redness, heat, tumefaction, furring of the tongue, and local discomfort constitute the symptoms witnessed in light cases; but in some, and particularly in infants, there is severe pain, sufficient, indeed, in the majority of cases to prevent nursing. Craving for cold drinks and perverted taste are nearly always noted. Local pain also attends a form of stomatitis observed in nursing women. In severe cases of catarrhal stomatitis the tongue appears enlarged and the lingual papillæ project prominently. The saliva is

greatly increased in quantity and is often sufficiently acrid to excoriate the lips and chin. Minute areas of the epithelial covering often become transformed into small, shallow, pul-taceous, and quite painful ulcers, which are especially sensitive when touched or brought into contact with other mucous surfaces during mas-tication. An alkaline reaction of the saliva is usual during the ulcerative stage. Slight fever is sometimes present even in the condition occurring independently of infectious febrile disorders, of which catarrhal stomatitis is a frequent complication. The symptoms usually last from four to ten days.

The general condition is rarely disturbed except when the stomatitis is secondary to inflammations in other parts of the alimentary tract or to the specific infectious fevers.

In some instances the oral mucous membrane is dry, the inflammation manifesting itself by the presence of heat, pain, and redness. This constitutes the "erythematous catarrhal stomatitis" of certain authors.

ETIOLOGY AND PATHOLOGY.

—Catarrhal stomatitis may be primary or secondary. In the primary form the causative factor is a local irritant, —mechanical, chemical, or thermal,—which gives rise to excessive des-quamation of the epithelium. Undue acidity of the oral secretions, unduly hot or cold foods, tobacco, strong condiments, fermenting or decomposing particles of food through insufficient cleansing of the mouth and teeth, dental caries, etc., may give rise to the affection. In the secondary form the oral inflammation is symptomatic and often attends infectious diseases,—measles, typhoid fever,—

and other exanthemata, and the prolonged fevers. It may also arise through continuity of tissue or by infection, owing to the presence in neighboring structures of an acute inflammatory disorder, such as tonsillitis, gingivitis, pyorrhea alveolaris, etc. Gastric disorders are frequently complicated with catarrhal stomatitis. This oral disease may also occur as an evidence of general depravity of the organism the result of unhygienic surroundings and poor food.

In the true catarrhal form thickening and softening of the mucous membrane is the most evident pathological feature, epithelial erosions covered with pul-taceous masses of cells undergoing retrograde metamorphosis being observed in various spots in marked cases. Leucocytes and red blood-cells are sometimes present and usually *Leptothrix buccalis*, micrococci, and bacilli are also to be found. The saliva is usually acid in reaction.

TREATMENT.—After proper hygienic conditions have been established and all irritant influences removed, the treatment should be mainly local. The internal administration of **potassium chlorate**, frequently resorted to, is a pernicious practice in this form of stomatitis, owing to its evil influence upon the kidneys. Employed in the form of a solution (about 1 dram—4 Gm.—to the pint—500 c.c.) as a mouth-wash, however, it is exceedingly useful. In many cases **sodium borate**, 10 grains (0.6 Gm.) to the ounce (30 c.c.), is more effective, employed frequently during the day, every half-hour, and with especial care after eating. In infants the mouth should be gently cleansed after each feeding

and a preparation of **boric acid**, 15 grains (1 Gm.) to the ounce (30 c.c.) of rose-water, applied with a swab, or, better, on a square piece of soft linen over the finger of the nurse. When cold drinks are ungrateful and the inflammation intense and protracted, the use of **hot milk** and **lime-water**, **mucilaginous decoctions**, and **sedative sprays** of 1 or 2 per cent. solutions of **cocaine** or **phenol**, or astringent solutions of **silver nitrate** ($\frac{1}{4}$ to 1 per cent.), **alum** (5 to 10 grains to the ounce of honey), or **glycerite of tannin** (2 drams—8 Gm.—to the ounce—30 c.c.—of water), are useful, especially where there is a tendency to chronicity. When mastication is difficult or very painful, the local application of a 4 per cent. solution of **cocaine** to the sensitive spots affords great relief and enables the patient to eat comfortably. When the shallow ulcers resist less active measures they should be lightly touched with **copper sulphate** or a weak solution of some one of the **silver salts**, preferably the **nitrate**.

Tender or spongy gums are greatly benefited by the use of a mixture in equal parts of the **tinctures of myrrh** and **krameria**, applied with a camel's-hair brush.

Where the condition occurs in a child, cleanliness of the mouth and nipples is of the utmost importance. The mouth should be cleansed after each feeding with cotton wrapped upon a small rod, or by inducing the child to suck **ice-water** from a piece of soft linen. **Food**, as far as possible, should be given **cold**, but the child should not be taken from the breast. If the disease persists, the mouth should be penciled with a $\frac{1}{2}$ per cent. solution of **silver nitrate** daily, and

cracks or ulcerations touched with the mitigated stick.

Internally, small doses of **aconite** or **potassium citrate** for the pyrexia, with minimum doses of **bromides** for the irritability and sleeplessness, may be required. An associated gastrointestinal catarrh may need correction through the use of **laxatives** and the administration of **bland foods**. Mild **tonics** should be used during convalescence.

APHTHOUS STOMATITIS.

SYMPTOMS.—In this variety of stomatitis there appear, besides the more or less marked inflammation of the oral mucosa, small, elevated, round or oval vesicles 2 to 5 mm. wide, and surrounded by a red areola, which, as early as twenty-four hours after their appearance, form shallow, yellowish-white spots of ulceration, with bright-red margins. They may appear singly or in groups in any part of the mouth, but they are apt to appear in greatest number on the labial mucous membrane, along the external portion of the gums, inside the cheeks, and along the edges of the tongue. The aphthæ may become confluent and give rise to large, irregular ulcers, the *confluent form* of stomatitis aphthosa. They are much more painful than those observed in the catarrhal form, and render nursing or the taking of food very difficult. The aphthæ sometimes extend to the fauces.

The general symptoms are somewhat more marked than in the previous form. Slight fever, anorexia, furring of the tongue, and heavy breath represent, however, about all the manifestations usually witnessed. Although there is an increased flow of saliva, the latter is never fetid

(Holt). The pain attending the presence of the ulcers renders the child especially cross and fretful when food is taken, but the active nervous manifestations of the more severe forms are absent. In the form observed in connection with febrile diseases the general symptoms are obviously those of the causative affection. Aphthous stomatitis tends to recur when the primary general cause is not completely removed.

ETIOLOGY AND PATHOLOGY.

—Aphthous stomatitis is usually observed in children under 3 to 6 years old, but is not rare in adults. It is a frequent complication of gastrointestinal disorders and is often seen in debilitated or poorly fed subjects, in tuberculosis, in anemia, and during dentition. It is most frequently met with in conjunction with, or as a sequel of, some febrile diseases, especially the acute exanthemata.

Local outbreaks of aphthous stomatitis have been traced to milk of cattle infected with foot-and-mouth disease (Ollivier).

No parasite special to aphthous stomatitis in general has as yet been isolated. The exciting causes are supposed to consist of certain deleterious substances, bacterial or toxic.

TREATMENT.—The treatment of this condition does not differ from that previously described. Proper **hygiene**, absolute **cleanliness of the mouth**, and the use of **bland foods** are important. Holt advised that each ulceration be touched with **silver nitrate**, but that no other active measures should be employed. The disease tends to spontaneous recovery in from seven to fourteen days. Goppert has recommended **orthoform** as a local anesthetic, the powder being

simply blown over the diseased areas, after cleansing the whole oral cavity. Food may be taken not sooner than 15 minutes after each application. Marfan resorts to frequent washing of the mouth with a saturated **boric acid** solution or a 1:500 solution of **phenol**. To the ulcers he applies a 5 per cent. solution of **silver nitrate**, a 1:500 solution of **potassium permanganate**, or a solution of **iodine** and **potassium iodide** in glycerin and water.

The following preparation is much employed by French clinicians:—

R Sodium borate 4 parts.
Tincture of benzoin 2 parts.
Distilled water 10 parts.
Syrup 20 parts.

M. To be applied five or six times a day.

Swab applications of 4 per cent. **cocaine** solution may be necessary when the pain is very intense. In the confluent form **sodium salicylate** solution—1 dram (4 Gm.) to the ounce (30 c.c.) of water—used locally is recommended, and **potassium chlorate** in small doses in solution, as well as in the dry powdered form applied to the ulcers, is beneficial. Symptomatic treatment should be instituted as required.

ULCERATIVE STOMATITIS (FETID STOMATITIS; PUTRID SORE MOUTH).

DEFINITION.—Inflammation of the mucous membrane of the mouth and underlying structures, attended by the formation of a deep ulcer which usually develops in the gum about the lower incisors. It only occurs when there are teeth (Forchheimer).

SYMPTOMS.—Ulcerative stomatitis generally develops near the edge of the gum immediately above the labiogingival sulcus. The area af-

fectured is at first red and tumefied and very sensitive. A deep, pus-secreting ulcer having a red areola, surrounded, in turn, by a zone of edema, is soon developed. In some cases this ulcer reaches down to the periosteum, and is followed by necrosis of the alveolar process. The gingival mucous membrane becomes softened and spongy and the teeth are loosened. Although the inflammatory process may invade all the tissues of the mouth, the ulceration rarely extends beyond the anterior portion of the gums. Occasionally the membrane of the cheek opposite the ulcerated area also ulcerates. The breath becomes intensely foul, and slight gingival hemorrhages cause the profuse saliva secreted to appear bloody. Severe pain is experienced during mastication. There are swelling and pitting of the tongue and enlargement of the submaxillary glands. Vomiting, diarrhea, and marked fever are usually present, and an exanthematous eruption resembling that of measles is occasionally observed. In children the disease sometimes culminates fatally, especially when unhygienic environments and unwholesome food cannot be corrected.

ETIOLOGY AND PATHOLOGY.

—That a specific bacterial cause must exist is emphasized by the occasional prevalence of ulcerative stomatitis as an epidemic disease in institutions, barracks, camps, and prisons, especially when the sanitary conditions are defective and where poor food is supplied. Squalor in all its forms tends to promote its appearance, cold, damp, and defective ventilation being among the many predisposing elements. Tartar accumulations, carious teeth or decaying roots, infectious diseases, congenital

heart affections (Duckworth), scurvy, and saturation with lead, mercury or phosphorus are etiological factors.

In many instances the organisms of Vincent's angina—a fusiform bacillus in conjunction with slender spirochetes—seem to bear a causal relationship. Amebæ may be present in addition. In the form known as *trench mouth*, there is an affection of the gums, tongue and mucous surfaces of the cheeks and tonsils, with early appearance of ulcers covered with a white, friable membrane, less adherent than in diphtheria. Coupled with this are a fetid breath, salivation, loosened and tender teeth, and bleeding of the gums. Occasionally a gangrenous process follows.

TREATMENT.—In this affection **potassium chlorate** given internally, 2 to 5 grains (0.12 to 0.3 Gm.) three times a day to a child, and also applied locally in the form of a mouthwash, is very useful. Internally, it is best given in a 3 per cent. solution with a little syrup, $\frac{1}{2}$ to 1 teaspoonful every two hours. Its toxic effects, if used in too large quantities, should not be forgotten. In obstinate cases, application of a solution of **silver nitrate** may be useful.

In trench mouth, local use of a mixture in equal parts of **Fowler's solution** and **wine of ipecac**, with a little glycerin added, proves effective. **Arsphenamin** applications and freezing with **ethyl chloride** have also seemed valuable.

In cases of pneumococcic origin, local use of **ethylhydrocupreine (optochin) hydrochloride** is advised.

A 1-grain to the ounce solution of **potassium permanganate** is sometimes required to counteract the foul breath, and the nitrate of silver stick

applied to the edges of the ulcers hastens recovery. **Hydrogen dioxide**, 1 dram (4 c.c.) to the ounce (30 c.c.), is preferred by some clinicians as a mouth-wash. Kissel's procedure in obstinate cases is to **urette** the ulcers daily and rub into them powdered **iodoform**. Care should be taken to preserve teeth that are loosened by special attention to the surrounding gums; the latter should, besides being kept scrupulously clean, be occasionally painted with a 20-grain (1.3 Gm.) to the ounce (30 c.c.) solution of **alum**. Pieces of necrosed bone occasionally keep up the ulcerative process. The cavity from which the pus oozes should be carefully probed and surgical removal resorted to if needed. A **tonic** treatment should be instituted. The **syrup of iodide of iron** is especially valuable; **codliver oil** is preferable in poorly nourished children. **Hygienic surroundings** and **wholesome food** should be insured. The disease is contagious and proper **isolation** methods should be put in practice.

PARASITIC STOMATITIS (STOMATITIS MYCOSA; THRUSH; SPRUE; MUGUET; SOOR).

DEFINITION.—A disease characterized by the formation upon the mucous membrane of the mouth of pearly-white spots or flakes which gradually increase in size and spread to adjoining structures and organs.

SYMPTOMS.—This form of stomatitis usually begins upon the tongue, and, spreading in every direction, may gradually involve the lips, the cheeks, the palate, the gums, the tonsils, the pharynx, the larynx, and even the gastrointestinal tract down to the ileocecal valve (Parrot). The

superficial lesion appears as small, grayish-white spots, surrounded by a zone of blood-vessels. These soon become elevated, increase in size, and often coalesce to form a false membrane; this, in some instances, has a characteristic filmy, or lace-like, look; in others it stimulates a thick, friable pseudomembrane (Holt). These areas or flakes may be readily brushed off, leaving no appreciable mark upon the surface from which they were removed. Sometimes the flakes appear yellowish or brown, and the seat of implantation bleeds, shallow erosions being then perceptible. The constitutional symptoms are less marked than in the other forms. The local manifestations are comparatively benign. Indeed, dryness of the mouth and local heat, difficult nursing or feeding owing to more or less great tumefaction and stiffness of the mucous structures, represent about all the discomfort complained of. Still, the disease is a stubborn one and the lesions may persist for months. A fatal issue is occasionally witnessed in debilitated children.

ETIOLOGY AND PATHOLOGY.

—The primary factors in the development of parasitic stomatitis consist of an abnormal condition of the oral mucous membrane, upon which is superimposed the influence of the *Saccharomyces albicans*. This fungus develops from round or oval spores into long, branching mycelial filaments requiring an acid medium and at no time growing upon the normal mucosa. Such a condition may be especially brought about in infants by unclean feeding-bottles when impaired general nutrition coexists. Sweets, fermenting bits of acid food, and uncleanliness of the mouth may act as

exciting causes by acidifying the normal secretions: a condition which the growth of mycelium intensifies. The transmission of the thrush spores by means of feeding-utensils, spoons, cups, feeding-bottles, etc., accounts for the epidemics occasionally observed.

The predisposing factors are mainly those which tend to lower the general vital tone: the exanthemata, hereditary syphilis, etc.; but it may also appear in apparently robust children. Parasitic stomatitis is likewise met with, in adults, as a complication or sequel of infectious fevers and diathetic diseases—cancer, tuberculosis, etc.

The fungus develops among the epithelial cells and acini of the mucosa, forming a dense network. It may be readily recognized microscopically if the diagnosis be at all doubtful.

TREATMENT. — Prophylactic measures are first in order, the causative factors being eliminated as far as possible. **Cleansing the mouth and all utensils used, and sterilization of feeding-bottle and all other feeding-instruments** each time they are used are imperative, to prevent reinfection. The first should be done gently, but thoroughly, four or five times a day. The next step is to counteract the acidity of the oral secretions by the frequent use of **alkaline washes and beverages**. **Sodium borate**, 20 grains (1.3 Gm.) to the ounce (30 c.c.); **sodium sulphite**, 60 grains (4 Gm.) to the ounce; a saturated solution of **potassium chlorate**, and pure **lime-water** are useful as mouth-washes. In some cases, especially where fetor of the breath is present, a 1 grain (0.06 Gm.) to the ounce (30

c.c.) solution of **potassium permanganate** or a solution of **hydrogen dioxide** is more effective, used hourly. The atomizer is sometimes convenient. Applications of 3 to 5 per-cent. **silver nitrite** solution are beneficial in stubborn cases.

To alkalinize the beverages, **lime-water**, 1 to 4, may be added to the milk, in the case of infants.

Lavage of the infant's stomach with an **alkaline mineral water** has been advocated by Steinert; likewise, the sucking of a **boric acid teat**. Maier advises local applications of 0.5 to 1 per cent. **acriflavin** solution.

Sugar and sweets, starchy food, and all syrupy excipients, when remedies are prescribed, **should be avoided**.

In some instances all the local measures will fail until a **change of air, good food, and tonics** have greatly improved the general health. Minute—*i.e.*, tonic—doses of **calomel** or **mercury bichloride** are valuable in this connection.

GANGRENOUS STOMATITIS (NOMA; CANCRUM ORIS; WANGENBRAND).

DEFINITION.—A disease usually observed in children, from 2 to 5 years old, in which a gangrenous process begins on the gums or inner side of the cheek and spreads with rapidity.

SYMPTOMS.—Gangrenous stomatitis begins almost always during convalescence from an acute febrile process in unusually debilitated children, the first lesion being a small nodule, dense and sensitive, appearing on the gum or the cheek. The skin and the neighboring mucous surface become rapidly hard and swelled or there is edema. There may be pain, but, as a rule, little discomfort. In mild cases

the primary ulceration may be limited to one of the starting points and finally heal under local treatment, leaving the parts deformed and the patient disfigured if penetration of the cheek has occurred; but in the vast majority of instances the necrotic process rapidly extends, the cheek is perforated, and the chin, the tongue, the jaws, and remote structures—such as the eyelids and ears—are involved in the destructive process.

Violent systemic manifestations are present. There are marked fever and practically intractable diarrhea, the breath becomes intensely foul, and the submaxillary and cervical glands are more or less enlarged. Edema of the feet and delirium are common. The prostration soon becomes alarming and all the evidences of fatal marasmus appear. The disease is usually fatal in from one to two weeks, but the patients are often carried off by affections that appear as complications—aspiration pneumonia, pulmonary gangrene, enterocolitis, endocarditis, etc. In short, the phenomena are those of a violent septicemia.

ETIOLOGY AND PATHOLOGY.

—The affection occurs in poorly fed children, especially girls living in damp, filthy quarters, and children recovering from various infectious diseases, especially measles, scarlatina, diphtheria, and typhoid fever. It is essentially a disease originating primarily in lowered vitality, and is not observed in vigorous healthy children.

The complications observed are usually ascribed to metastatic infiltration of the distant structures involved, except in the case of pneumonia, which is due to aspiration of gangrenous matter, and enterocolitis, due to the ingestion of gangrenous

detritus. A bacillus resembling that of diphtheria has been isolated by Bishop, Ryan, and Schimmelbusch. Many believe, however, that Vincent's fusospirillar combination, which is often found in the tissues, together with many other organisms, is the most important exciting factor.

TREATMENT. — Prophylactic measures are also of primary importance in this form of stomatitis. The child's diet should at once be changed to one calculated to increase general nutrition. **Nux vomica** and **gentian**, combined and in small doses, or **strychnine**, are advantageous to promote appetite. Strong **beef-juices**, **peptonized milk**, or **koumiss** should be given every two hours.

Some recommend the early use of fairly large doses of **diphtheria anti-toxin** in every case of the disease and I have witnessed the case of a female adult who recovered under this treatment.

The local treatment consists in the destruction of the sphacelous areas by **caustics** after thorough cleansing. For the latter purpose a 1:500 solution of **potassium permanganate** is very useful, but **hydrogen dioxide**, **mercury bichloride**, or **phenol** solutions are preferred by some. These may be applied with an atomizer emitting a coarse spray. The **sloughs** must be thoroughly removed and the **bottom of the ulcer** fully **exposed**. This having been accomplished, a 10 per cent. solution of **cocaine** is applied to the wound, and after four or five minutes the latter is touched with pure **lactic acid** by means of a small cotton pledget wrapped around the end of a thin probe (Sajous). Every part of the cavity must be cauterized. This is to be repeated daily until

signs of resolution appear. **Nitric acid**, the **galvanocautery**, and the **Paquelin cautery** have also been recommended, but their use is more difficult. **Excision** under anesthesia is a safe and useful procedure. **Bromoform** and **bismuth subnitrate** are valuable to enhance the curative process when dusted on the cauterized ulcers. **Scrupulous cleanliness** of the **mouth** is imperative.

Mild **antiseptic washes** should be used frequently, and for the diminution of the fetor antiseptic **charcoal poultices** containing **boric** or **salicylic acid** are useful.

In favorable cases healing should be promoted by means of **stimulating antiseptic lotions** or **balsams**.

MERCURIAL STOMATITIS.

(See **MERCURY**, Vol. VI.)

ANOMALOUS FORMS OF STOMATITIS.

MEMBRANOUS, OR CROUPOUS, STOMATITIS.—True croupous stomatitis is always a complication of croupous angina, the membrane developing simultaneously with that of the tonsils. Diphtheritic stomatitis is rarely primary, but a complication of diphtheria of the fauces.

What is often called "membranous stomatitis," however, is but an aggravated form of aphthous stomatitis. The local inflammation is more intense: the aphthæ assume a development suggesting the presence of a diphtheritic or streptococcic pseudomembrane, while the ulcer, when the latter is removed, is deeper and larger. It is mainly observed in infants suffering from inherited syphilis or gonorrheal infection. In the adult it is occasionally caused by the local use of strong caustics. The treatment does not differ from that of

aphthous stomatitis, care being taken, however, to remove as far as possible the causative disorder.

FOOT-AND-MOUTH DISEASE, EPIDEMIC STOMATITIS, OR APHTHOUS FEVER.—An affection observed in lower animals (cattle, sheep, pigs, goats), and caused by an unknown micro-organism, is occasionally witnessed in the human being, particularly in children, the toxic element being transmitted through contaminated milk, cheese, or butter, or by inoculation while milking. The disease is said not to be transmitted through the meat of diseased animals.

SYMPTOMS.—The incubation period lasts from three to five days. The onset is marked by a rigor or mere slight shiverings, followed by fever and malaise. There are marked fever and gastrointestinal and bronchial irritation; a vesicular eruption appears upon the lips, mouth, and pharynx early in the history of the disease. The mouth is hot, the mucous membrane reddened and swollen, and salivation present. A miliary eruption, which may become pustular, may appear on the skin, especially on the fingers and hands. The tendency to hemorrhage is greater than in ulcerative pharyngitis.

DIAGNOSIS.—This is readily made from the prevalence of the disease in lower animals and the appearance of the eruption only in the mouth and extremities. Gerlach, who reproduced the disease in guinea-pigs by inoculation of the skin of their feet, advocates this test for diagnosis.

PROGNOSIS.—This is generally favorable, the course averaging 2 weeks.

TREATMENT.—The treatment indicated is that recommended in the

ulcerative form. Prophylaxis requires the use of **milk from healthy animals**, proper **stable hygiene**, and **isolation of diseased animals**.

Bednar's Aphthæ.—This is characterized by the presence, over the posterior part of the hard palate near the gums of infants, of white patches, or aphthæ, which sometimes overlie deep ulcers, the latter at times involving the bone. It is usually ascribed to the use of artificial nipples, to traumatism, such as that produced when the mouth is roughly cleansed by the nurse, or to the pressure of the tongue upon the mucous membrane while nursing. This form of stomatitis is overcome with difficulty. A **shorter and softer nipple** should be ordered when this cause is apparent and the measures indicated in ulcerative stomatitis resorted to.

Riga's disease (aphtha cachectica) has been observed almost exclusively in the southern provinces of Italy, where it seems to be endemic, occasionally attacking all the children in a family, whether the parents be healthy or not. It is observed: when the first teeth make their appearance, apart from whooping-cough, sometimes in children whose general health shows nothing wrong, sometimes in cachectic children who are exhausted by ordinary attacks of gastrointestinal catarrh. It begins as an ulceration under the tongue, close to the frenum. It is about the size of a flaxseed, and gradually enlarges to the size of a sixpence. It is gray in color and painless. The border is irregular and not sharply marked, and extends somewhat over the sound tissue. It may cause death, or, after a long time, recovery may take place. The children waste in flesh, their skin

becoming of an earthy hue. Enlargement of the liver and spleen occurs. There is no fever. Beginning at the age of 3 or 4 months, it frequently lasts until the twentieth month. It is mostly hereditary, and only seldom do the children of such families live, unless nursed at the breast of a healthy woman.

Parrot's Disease.—This disorder is observed in the newborn and debilitated children, and is characterized by the presence on both sides of the middle line of the hard palate of symmetrically disposed ulcers, which tend to increase in size. The ulceration often penetrates the underlying soft tissues to the bone, causing necrosis. It is a stubborn affection and requires the active measures advocated under ulcerative stomatitis.

Herpes zoster, or zona, of the mouth, as described by Hugenschmidt, is an inflammatory affection of one part and only one side of the buccal cavity, characterized by an eruption of herpetic vesicles, disposed in groups according to a regular direction. The eruption is preceded and accompanied by a neuralgic pain of the whole fifth nerve. The evolution of the disease may be divided into two periods: (1) the period of invasion; (2) the period of eruption. 1. Period of invasion begins by a rise of the temperature; there is fever; then headache, nausea, loss of appetite, etc.; intense neuralgia of the whole region of the fifth nerve. Fever lasts three days, and is followed by the period of eruption. 2. In period of eruption parts to be involved become excessively painful to the touch; mucous membrane is red and presents a series of little herpetic vesicles, disposed in groups and having size of a

pinhead; some of them are united. They assume a regular direction: usually the course of the nerve. No vesicles are to be found disseminated in the mouth. The neuralgia, which is general for the first three days, localizes itself as soon as the eruption occurs.

Very similar is a disorder described by Jacobi, also characterized by an herpetic eruption, and observed in neurotic subjects. In some cases it accompanies erythema multiforme. The treatment indicated is that of the general disorder.

La Perlèche.—This is a contagious disease characterized by the presence of ulcerations at the angle of the mouth. The probable cause is bacterial infection from drinking vessels.

Small elevations and fissures, resembling those of congenital syphilis, are seen at the angles of the mouth. When the mouth is opened these are stretched, causing smarting pain and bleeding. This causes the patient to lick the part and add more infection.

Burnt alum, silver nitrate, and covering the part with **bismuth** or **zinc oxide** are the most useful remedial measures.

LIPS, DISEASES OF.

INFLAMMATION, CRACKS, AND FISSURES.

Inflammation frequently occurs independently of oral or general affections as a result of cold during the winter months. When the slight vascular turgescence present is complicated with cracks or fissures, considerable discomfort results. Of diagnostic importance, however, is the fact that fissures, which are usually situated in the middle of the lips,

often betoken a strumous diathesis; enlarged cervical glands are, however, usually present in such cases. Again, cracks at the angles of the mouth suggest the possibility of general syphilis; the surrounding tissues in that case often appear sodden, while the fissure is apt to contain pus. Labial fissures are also often witnessed in women who, in threading a needle, first bite the thread and drag it between the lips before passing the tip through the eye (Jamieson).

TREATMENT.—Uncomplicated congestion of the lips soon yields to mild **astringents** or to a preparation such as the following, in which a resinoid substance is contained:—

R Tincture of benzoin,
Glycerinof each ℥ss.
Rose water, enough to
make℥iv.

When slight fissures or cracks are present, **rose-water ointment** or 10 grains (0.6 Gm.) of **salicylic acid** to the ounce (30 Gm.) of **cold cream** usually brings about prompt resolution. Fissures often resist all simple measures, and require the application of solid **silver nitrate** or powdered **alum**. In children persistent fissures leave deep furrows, and are apt to produce slight deformities. They should, therefore, be scraped with the **curette** under local anesthesia, and the edges of the wound drawn together and held in position by means of **court-plaster** until healed.

HERPES LABIALIS (FEVER BLISTER). See **HERPES**, Vol. V.

TUMORS OF THE LIPS.

Of all primary neoplasms, about 3 per cent. originate in the lips; but these structures show a higher percentage when cancer is alone considered, viz., about 5 per cent. As

compared to other forms of tumor observed in this region,—papilloma, sarcoma, angioma, fibroma, and cystoma,—cancer is observed in 99 per cent. of cases.

CARCINOMA.—This variety of growth develops almost exclusively on the lower lip. Of 352 cases analyzed by W. R. Williams, 340 originated in this situation. Among 1193 instances studied by Fricke the upper lip was affected in but 63 cases. The predilection of this location for the development of cancer as regards sexes is as striking. In the series of cases just mentioned 94 per cent. occurred in males. It is essentially a disease of adult and advanced life, the average being about 60 years; but carcinoma has been observed long before the fortieth year, the limit usually accepted. Fricke's list ranged from 24 to 83 years. A large proportion of the cases were in laborers and farmers, and heredity seemed to play a minor rôle. Pipe-smoking appeared to be an important predisposing factor, wounds and abrasions coming next in order.

Symptoms.—A labial cancer may begin as a mere excoriation, fissure, or ulcer that will not heal; a small tubercle covered by a thick scab that recurs as soon as picked off, or as a warty growth. The ulceration gradually spreads and deepens, the surrounding tissues being infiltrated and hard. In many cases the carcinoma begins as an ulcerating induration. The ulcer gradually assumes the typical appearance of an epitheliomatous growth, with an irregular, sloughing base and abrupt, everted edges. When irritated by the injudicious use of caustics or "specifics," it tends to fungate and its growth becomes more

rapid. At this stage it usually becomes quite painful, and nutrition soon suffers through the inability of the patient to take sufficient food, and a state of marasmus soon becomes evident, owing to repeated hemorrhages, the ingestion of cancerous detritus, etc. General toxemia is by this time fully demonstrated by the patient's facies, and he sinks with increasing rapidity. As a rule, the development is very gradual, and the glands of the jaws are not involved early. Enlargement of these glands and even their induration do not necessarily imply carcinomatous infiltration; but such glands should be removed whenever possible.

Diagnosis.—Whereas carcinoma occurs almost always in men, chancre of the lip is more frequently observed in women, and may occur at any age. The progress of cancer is slow, whereas chancre advances rapidly, lasts but a few weeks, and the glands are soon involved. The local Wassermann reaction and examination for spirochetes are of assistance. Ultimately the secondary manifestations appear in syphilis.

Prognosis.—Properly treated in its early stage, cancer of the lip is almost entirely within our control. Of 93 cases in various stages treated surgically and reported on by Sistrunk, 90 per cent. were well after 5 years (this excludes, of course, the advanced cases deemed inoperable when first seen). Pfahler has reported 80 cases treated by electrocoagulation and radiation, of which 74 recovered and were well several months to 18 years later, while in 2 the treatment failed, 2 recurred, and in 2 the result was unknown.

The prognosis is influenced by the

presence or absence of involvement of the submental and submaxillary glands or of thoracic lymphatic involvement.

Treatment.—Of all cancers, that of the lip has shown the least tendency to recur after **surgical removal**. Surgery is particularly indicated in the commonest form—the pearl or prickle cell type—which is more refractory to radiation than the basal cell epithelioma. There is no unanimity of opinion as to the indications for the **X-ray**, **radium** or **electrocoagulation**. There have been many favorable results from radium in cases without metastases, with a minimum of scarring and deformity. In cases with early metastases, if the glands do not subside under radiation of the neck, **radium implantation** may be tried or a **block dissection** done (Pancoast).

MISCELLANEOUS GROWTHS.

Nevi (see BLOOD-VESSELS, TUMORS OF, Vol. II) of the lip are sometimes witnessed. As a rule, they are small and may generally be removed by **ignipuncture** with a fine galvanocautery knife or by **electrolysis**. The latter is slower, however. **Dissection**, as if the growth were malignant, is sometimes necessary.

JAWS, DISEASES OF.

ALVEOLAR ABSCESS.—A suppurative dental periostitis due to diseased teeth. The simplest form, in which there is inflammation between the bone and the gum externally to the root of the tooth, is known as a **gum-boil**. The condition is generally quite superficial, and gives rise to but few external signs. When it is due to a disorder at the root of a tooth a true alveolar abscess is formed and the active manifestations are accom-

panied by severe throbbing pain, considerable swelling of the cheek of the corresponding side, and by protrusion of the tooth from thickening of the peridental tissues. When the lateral incisors are involved, the abscess may spread posteriorly between the layers of the hard palate, or anteriorly in the direction of the nose, opening into the latter. When the molars are involved, it may penetrate the tissues of the face, thus leaving a sinus or scar. Necrosis and pyemia have occurred in rare instances as complications.

Treatment.—The old-fashioned linseed-meal poultice is worse than useless, tending to encourage the inflammatory process and to involve the cheek. **Water** as hot as can be borne, held in the mouth, is far better. Painting the gums with a 10 per cent. solution of **cocaine** is sometimes temporarily effective in mild cases. **Free lancing** should be resorted to if the abscess progresses. Where spontaneous rupture externally is inevitable an incision should be made over the abscess. If these measures do not suffice the patient should consult a dentist.

EPULIS.

Although applied to various neoplasms of the gums, the term "epulis" is correctly applicable only to a growth of the alveolar process and tooth-sockets. Two varieties are recognized: *simple*, or benign, and *malignant*.

Simple Epulis.—A benign epulis is, in reality, a fibroma: a smooth, rounded projection of the gum, usually beginning between two teeth, which it gradually separates, displaces, and loosens. It may involve several teeth and involve the posterior or the anterior aspect of the alveolus.

It is painless, of slow and indolent growth, but, if left to itself, it ulcerates and causes marked deformity. It sometimes ossifies or becomes sarcomatous.

Malignant Epulis.—This is a much more dangerous variety. Beginning usually at the socket, it is characterized by the presence of an irregular, multinucleated mass of giant cells associated either with round or spindle cells, or both. It is really a myeloid sarcoma. It is exceedingly vascular, purplish red, grows much more rapidly than the simple epulis, and is finally transformed into a spongy mass, which projects in various directions and bleeds upon the least contact with a hard substance.

TREATMENT.—Whether the growth present be a simple or malignant one, the sooner it is removed, the better. The tumor, and the tooth or teeth and the portion of the alveolar process involved, should be **excised**, this constituting the only safe mode of treatment. Mere scraping is followed by a return of the tumor in almost every case, whether simple or malignant. The portions of bone to be removed being mapped out, two vertical incisions are made with a Hey saw, and the diseased mass is removed with forceps, after having been dissected from its surroundings.

NECROSIS.

Necrosis of the jaw may be due to any condition liable to give rise to inflammation of its periosteum by injury due to the extraction or improper manipulation of teeth, by various suppurative diseases, the acute exanthemata, pyemia, actinomycosis, etc., or by the action of various diathetic processes, such as syphilis, tuberculosis, or leprosy. It is most fre-

quently caused by the fumes of phosphorus (see beyond), and by mercury taken internally. Deficient nutrition, scorbutus, or other conditions in which the organism is deprived of its vital pabulum frequently manifests necrosis of the jaws as a symptom. It may thus occur at any age, and does seem to show a predilection for either the upper or lower maxillary.

Necrosis is always preceded by deeply seated and intense pain; the parts are red, inflamed, and tumefied. After a time the pain is somewhat reduced and sinuses are formed, from which a fetid pus exudes. The teeth are loosened and fall out, and the cavity left is bathed in pus. A probe passed into any of the sinuses reveals the presence of dead bone by conveying to touch the characteristic sensation of roughness. Portions of the bone become detached and are easily removed.

PHOSPHORUS NECROSIS.

SYMPTOMS.—Phosphorus necrosis comes on gradually, and sometimes long after the patient has been exposed to its toxic influence in connection with his occupation, the manufacture of matches, etc. But, once started, it progresses rapidly, involving large areas of bone; owing to the general toxemia, many foci of inflammation may be developed at once. The lower jaw seems to be that in which phosphorus necrosis most frequently occurs.

Pain is one of the earliest symptoms; at first intermittent, it soon becomes continuous. Suppuration of the perialveolar and peridental membranes occurs, pus appears at the alveoli, and the inflammation soon includes the gum structures, the tissues of the face becoming infiltrated, and

the characteristic deformity appears. The entire periosteal layer is then invaded; sinuses are formed, opening into the mouth and externally under the lower maxillary edge, and pus is exuded on all sides. The pain becomes less marked when this stage is reached, unless the necrotic process involves the condyle, when severe pain in the ear is experienced.

The general health of the patient soon suffers considerably. The constant discharge, the presence of offensive pus in the mouth and stomach (much of the discharge being swallowed), the occlusion of the jaws through infiltration of the maxillary muscles, and the impediment to the ingestion of food combine to rapidly bring on exhaustion and death unless proper treatment is instituted.

In some cases, however, the process is a slow one, and comparative health is enjoyed, while now and then a necrotic sequestrum is discharged through one of the sinuses.

In some operatives, however, a special susceptibility to phosphorus exists, and acute symptoms—nausea and vomiting, etc.—indicate an acute poisoning that requires immediate cessation of all work in which phosphorus is handled or inhaled.

ETIOLOGY AND PATHOLOGY.

—The inhalation of the vapor of phosphorus and the particles of this substance taken in with the food when the hands are not properly cleansed and improper care of the teeth combine to very gradually bring on the general toxemia. This, in turn, gives rise to slow disintegration of the red blood-corpuscles and fatty degeneration of the arterial coats. That the maxillary bones should, of the entire osseous system, bear the

brunt of the disease demonstrates that a local factor must play a prominent part in the disease. It is thought that the periodontal membrane laid bare by accumulation of tartar, and whose vascular supply is already diseased by the general toxemia, is easily influenced by any phosphorus that may enter the mouth, and thus readily yields to the irritation induced, carious teeth, and other infectious foci, and that the necrotic process follows the local inflammation engendered.

TREATMENT.—In the early stages the teeth should receive careful attention, **carious ones** being **extracted**, while the **tartar** around those not diseased should be carefully **removed**. These manipulations should be conducted antiseptically, strict **care of the teeth** following.

Turpentine, according to Hohler and Schimpf, when exposed some time to the air becomes rich in ozone, and prevents fatty degeneration. Theoretically, it is thus capable of neutralizing the effects of phosphorus, a power which has also been demonstrated practically. Andant found that it arrested the vapor of phosphorus in the dark. The ordinary American oil of turpentine is of no value, however, unless it be long exposed to the air. It is to be administered internally and by inhalation. **Potassium permanganate** is also a useful antidotal agent. **Lime-water** and **magnesia** are said to be helpful in preventing the drug from affecting the tissues. The general health should be carefully watched and every means used to facilitate increased nutrition by the use of **tonics** and **easily digested foods**.

In the stage of ulceration **antiseptic**

washes as warm as possible should be frequently used. A weak **potassium permanganate** solution is particularly valuable in this connection, when syringed into the sinuses. **Iodoform gauze** can then be packed in to absorb secretions. **Sequestra** should be removed when free, and the cavity packed.

Relatively early **operative intervention** permits of better preservation of the periosteum, thus enabling new bone to form to replace partially that destroyed. In rare cases complete removal of the jaw is required.

When the lower jaw is involved, it is well to **remove** but half of the **ramus** at one time, in order to preserve the contour of the parts. After the expiration of eight or ten weeks the remaining portion may be removed.

When the patient cannot avoid exposure to phosphorus fumes, the preventive measures should consist in **free ventilation** and **absolute cleanliness**, especially of the **mouth and hands**.

J. MADISON TAYLOR

AND

FRANK E. FREEMAN,
Philadelphia.

MUMPS. See SALIVARY GLANDS, DISEASES OF.

MUSCLES, DISEASES OF THE.

MYOSITIS.

Inflammation of muscles may be primary or secondary, general or local, parenchymatous or interstitial, and suppurative or non-suppurative, the different forms running an acute, sub-acute, or chronic course. As a rule, only the voluntary muscles are involved, an exception to this being the heart muscle.

Owing to the obscurity regarding the etiology of certain forms of myositis, various classifications have been proposed. Lorenz divided the myositides into three groups,—suppurative, non-suppurative, and myositis with special terminal lesions. Batten gives three main groups,—primary, secondary, and myositis with special terminal lesions, placing the suppurative form in the second group, while Kader considered the advisability of including both the suppurative and non-suppurative forms under the general heading of infectious myositis.

Myositis sometimes occurs in the course of infectious diseases, such as typhoid fever, syphilis, tuberculosis, gonorrhea, actinomycosis, etc.

PRIMARY SUPPURATIVE MYOSITIS.—**Synonyms.**—Diffuse suppurative myositis; infectious myositis; idiopathic, acute, suppurative muscle inflammation.

Definition.—A bacterial infection of one or more muscles, usually running an acute course and terminating, as a rule, in suppuration.

Among 7 cases of infectious myositis, 4 were in children. Staphylococci were found in 3 cases, streptococci in 1, and both in 1. In 1 the pus seemed sterile, and in the 7th case the process underwent absorption without incision. The 2 cases with streptococci died; in both the autopsy revealed lung abscesses and in 1, also renal abscesses. G. Holm (*Acta chir. scandin.*, Oct. 18, 1924).

Symptoms.—The onset in primary suppurative myositis is like that of an acute infectious fever. It is ushered in by a chill, with rise of temperature, headache, and generalized pains, which are soon referred to the muscles. The affection may be limited to a single muscle, or many muscles may

be involved. Those affected are swollen, indurated, spontaneously painful, tender upon manipulation, and non-adherent to the surrounding tissues. The muscles are in a state of contraction, causing limitation of both active and passive movements. The overlying skin may be erythematous, but, as a rule, it is normal in appearance. Edema of the subcutaneous tissue may be present.

Any attempt to move the affected muscles causes severe pain and if the affection is at all general the patient soon becomes helpless. In a few days, in the great majority of cases, the indurated masses soften and signs of suppuration become evident. In a small percentage of cases resolution occurs without abscess formation.

Unless the pus is promptly evacuated there is danger of metastasis through infiltration of the pus into the surrounding tissues.

The muscles most frequently involved are those of the upper and lower extremities, chest, and lumbar region. One muscle alone is affected in the majority of instances, 2 frequently, and as many as 18 were found involved in one case reported.

Recurrence is rare, but the condition has been known to reappear after a few months' interval.

Diagnosis.—The pain and tenderness referred to the affected muscles and the characteristic induration and swelling conforming to the shape of the muscles, together with the abrupt febrile onset, should render comparatively easy the recognition of primary suppurative myositis.

Cases in which metastasis has occurred must be separated from the metastatic abscesses occurring in pyemia. In the latter affection the mus-

cular induration and contraction would be absent.

Suppurative myositis may superficially resemble osteomyelitis in cases where the abscess has broken through the muscle sheath.

Pathology.—The muscles affected vary in appearance according to the stage and intensity of the inflammatory process. Early they are dark red, later becoming grayish red from the infiltration and breaking down of the tissue. The muscles may show diffuse purulent infiltration, multiple small abscesses, or a larger solitary abscess. The abscess wall is composed of grayish-yellow, necrotic muscle tissue and the cavity filled with a thick, yellow or greenish-yellow pus containing necrotic tissue and sometimes blood. The abscess may be so large as practically to include the entire muscle. The overlying skin and subcutaneous tissues are, as a rule, uninvolved.

Microscopically, both interstitial and parenchymatous changes are seen. In the early stages the interstitial tissue may not show much change, but it is considerably increased in long-standing cases and may almost entirely replace the muscle tissue. The muscle fibers likewise may show but slight change, or may be swollen, with disappearance of the cross-striation (Scriba). There is usually a proliferation of the muscle nuclei, and vacuolic degeneration of the fibers has been observed (Lorenz). Round-cell infiltration is sometimes seen in the muscle sheath and interstitial tissue, and is always present in the tissue forming the wall of the abscess, which also contains bacteria.

Etiology.—Age, sex, and occupation play unimportant rôles in the causation

of primary suppurative myositis, except in so far as they predispose to overexertion, exposure, and trauma. These factors act by lowering the resistance of the muscles to infection, Miyake (quoted by Steiner) having shown experimentally that overuse of a muscle could cause separation of its fibers, with the occurrence of punctiform hemorrhages which offer a favorable site for the development of infection.

The pus from the muscle abscesses has been found to contain micro-organisms in almost every instance in which these have been searched for. Staphylococci, streptococci, a diplococcus resembling the pneumococcus, and an unidentified bacillus have been obtained in cultures from the abscesses by different observers. The *Staphylococcus pyogenes aureus* is the chief offender, having been found in pure culture in the majority of cases. The credit for the first reported finding of micro-organisms in primary suppurative myositis belongs to Scriba and Brunon.

The bacteria make their entrances chiefly through the skin by way of infected foci, less frequently through the mucous membranes, and from these ports of entry are conveyed through the blood-vessels to the muscles. The disease has been aptly described by Steiner as a "septicopyemic" infection.

While suppurative myositis has a widespread distribution, it is far more prevalent in Japan than in any other country, Japanese observers believing this is due to diet, climate, and racial peculiarities.

Prognosis.—The outlook for recovery is favorable if the condition is promptly diagnosed and properly

treated by **incision and evacuation of the pus**, recovery taking place in from six to twelve weeks. Unpleasant but fortunately rare sequelæ are muscle atrophy or deformities from contraction of scar tissue.

In cases which are unrecognized and in which rupture of the abscesses occurs, with subsequent formation of metastatic abscesses, the prognosis is obviously grave. Death may result from endocarditis or pneumonia.

Treatment.—At the onset, free **purgation** with the **local application of cold** may in some instances cause resolution without suppuration. **Free incision and drainage** are, of course, indicated as soon as fluctuation occurs. In the later stages of the disease **massage and passive movements** are of value in preventing contractures.

ACUTE POLYMYOSITIS.—**Synonyms.**—Dermatomyositis; dermatomucosomyositis; pseudotrichinosis.

Definition.—A disease characterized by inflammation of the skin and muscles, non-suppurative, and running an acute, subacute, or chronic course.

History.—The first accurate description of this disease dates from the cases published, with autopsy, by Unverricht (Münch. med. Woch., 1887, xxxiv, 488), Hepp (Zeit. f. klin. Med., 1887, xii, 533), and E. Wagner (Deut. Archiv f. klin. Med., 1886-87, xi, 241) in 1887.

The patients were aged 24, 36, and 34 years, respectively, and had in common inflamed, painful, and swollen muscles, with edema of the overlying subcutaneous tissue. Unverricht's case had an urticaria-like eruption, Hepp's patient an exanthem on the face and chest, while Wagner found an erysipelas-like dermatitis on each arm of his patient. Two of the 3 cases died of lobar pneumonia, the third in a suffocation attack. Varying degrees of muscle degeneration with interstitial round-cell infiltration and minute interfibrillar hemorrhages were found in each instance.

Report of 2 cases, both with the diagnosis confirmed by muscle biopsy. In 1 there was electrocardiographic evidence of myocardial involvement. In both, death occurred from pulmonary complications, in 1 instance after tonsillectomy. The disease is differentiated from polyneuritis by the absence of reaction of degeneration. Friedman (Med. Jour. and Rec., Mar. 17, 1926).

Symptoms.—The disease, as a rule, develops gradually with malaise, general weakness, anorexia, headache, and occasionally vomiting. Rarely this prodromal period is absent and the onset is more abrupt. Fever, usually moderate in degree and intermittent in character, soon appears; then local symptoms develop. Pain, at first vague, rapidly becomes referred to the muscles, group after group of which become successively involved. The muscles become tender and rigid; the extremities swollen and edematous. The edema may affect also the face and trunk.

An early and characteristic symptom is a dermatitis, which may be limited to areas over the affected muscles or may spread and become more general. It appears in the form of a rash, which varies in different cases. It may occur as an erythema resembling the skin appearance in erysipelas, as an erythema nodosum, an urticaria, or a roseola.

The spleen becomes enlarged and tender and albumin and hyaline and granular casts are sometimes found in the urine.

Stomatitis and ulceration of mucous membranes are not infrequent symptoms. Outside of the pain, sensory symptoms are not marked; paresthesiæ are sometimes present, but there is never any sensory loss. The inflammation may spread to the muscles

of deglutition, giving rise to difficulty in swallowing, and implication of the respiratory muscles sometimes causes death from suffocation or bronchopneumonia.

The reflexes are preserved, but may be difficult to elicit on account of the swelling and edema of the extremities. Electrical reactions are normal early in the disease, later showing a quantitative decrease (Oppenheim).

In the more severe cases atrophy of the muscles, with partial reactions of degeneration (Lewy), is occasionally seen, and a marked pigmentation may follow the dermatitis.

Diagnosis.—The diagnosis of dermatomyositis should not be difficult if the following characteristic features of the disease are borne in mind: the gradual onset, the dermatitis, the muscular pain and tenderness, and the edema of the subcutaneous tissue.

In trichinosis there would be a history of the patient eating raw or partially cooked pork, and the *Trichinella spiralis* would be found in the stools and in excised portions of the affected muscles. In long-standing cases a skiagram may show calcification in the sheath of the trichinæ (Batten). The initial gastrointestinal symptoms and a marked eosinophilia are also of assistance in the separation of this disease from dermatomyositis, and still another point in the differentiation is the early involvement of the eye muscles and of the diaphragm in trichinosis.

Neuromyositis presents symptoms of nerve involvement, as sensory loss, muscular atrophy, and absent knee-jerks, and dermatitis is absent.

Primary suppurative myositis has a more acute onset and exhibits infected

foci with abscess formation; bacteria are found in the affected areas.

In syphilitic myositis there would be a history of specific infection and the blood would give a positive Wassermann reaction.

Pathology.—Almost all the muscles of the body may be implicated, although the ocular muscles and the masseters generally escape (Batten). The changes that take place may be most marked in the parenchyma, or in the interstitial tissue, or they may be equally diffused. The affected muscles are swollen, lusterless, generally of a pale-red or yellowish color, and often covered with grayish or reddish patches or streaks. In consistency the muscles vary greatly; they may be hard and firm or soft and friable. Hemorrhages large enough to be visible to the naked eye are sometimes observed in the muscles.

Microscopically, changes have been found in the muscle fibers, in the interstitial tissue, and to a slight extent in the blood-vessels. The lesions may be localized or more or less widely diffused. The muscle fibers are swollen and present varying degrees of degenerative change, such as hyaline, granular, waxy, and rarely fatty. The striæ are generally absent or indistinct, and vacuoles are occasionally seen. In almost every case an increase of the nuclei is noted. Round-cell infiltration takes place between the fibers, especially in the vicinity of the blood-vessels, which are apt to be dilated and engorged. Hemorrhages form a part of the pathological picture in the majority of instances. In the subacute and chronic forms there is a marked connective-tissue increase, especially in the perimysium. It is probable that the changes in the

parenchyma are secondary to the acute interstitial changes (Pfeiffer, Lorenz). The subcutaneous tissues overlying the affected muscles show an inflammatory edema. The spleen is invariably enlarged and softened, and the lungs have frequently shown a bronchopneumonia at autopsy.

Etiology.—The cause of dermatomyositis is as yet undetermined. The disease has been variously considered as being (1) of toxic origin; (2) as being due to a vegetable parasite, and (3) as being caused by an animal parasite.

Senator (Deut. med. Woch., 1893, xix, 933) advocated the theory of a toxic origin, a case reported by him having developed the malady after eating stale crabs. Kell (Jour. Amer. Med. Assoc., 1896, xxvi, 967) added further support to this theory through the report of 3 cases occurring after partaking of fish. Unverricht suggested that the disease was due to an animal parasite belonging to the order Gregarinoidea, and later Lorenz found a sporozoön-like parasite in one of his cases. In the majority of cases examined, however, results have been negative; yet the rise of temperature accompanying the skin and muscle symptoms, and the constant finding of an enlarged spleen, certainly point toward a probable infectious origin. Nothing conclusive has as yet been advanced to indicate that the disease is contagious.

Blood-culture finding in a case of acute polymyositis which supports the view that this disease is a bacteremia due to a micrococcus, with rather uniform predilection for the musculature. The infection assumes the form of polymyositis when a *Micrococcus pyogenes* bacteremia occurs in a person whose condition favors rheu-

matism, although there is no pathological basis for this, as the lesions are different. Herbert Fox (Amer. Jour. Med. Sci., June, 1913).

Polymyositis occurs in the two sexes with nearly equal frequency, the malady slightly predominating in males. Age does not appear to be a very important factor, for although adults are most frequently affected, cases have been recorded occurring both in childhood and in advanced age.

The disease has a wide distribution, cases having been found in this country as well as in various countries abroad, England and Germany having contributed the largest number. Steiner has reported a case of polymyositis in a negro.

Prognosis.—The acute forms last from a few weeks to two months, chronic cases extending over a period of from one to two years, with the subacute forms running an intermediate course. Any case is apt to have remissions and relapses. That in Steiner's series of 28 cases 17 were fatal affords an idea of the seriousness of the affection, and even when recovery does occur there may be more or less muscular atrophy.

Treatment.—When the patient is seen early, relief of the pain is the first consideration. **Aspirin** and the **salicylates** are of some advantage, and in severe cases it may be necessary to resort to the administration of **morphine**. The **nutrition** of the patient should be kept up, and if pneumonia develops, it, of course, requires appropriate treatment. In the later stages of the disease **passive movements**, **massage**, and **electricity** are useful measures for the prevention or treatment of muscular atrophy.

MYOSITIS HEMORRHAGICA.

— **Synonym.** — Polymyositis hemorrhagica.

Definition.—A form of myositis characterized by the presence of intramuscular hemorrhage, usually having an acute onset, and running an acute, subacute, or chronic course.

History.—Vernon has the credit of placing, in 1888, the first case of this disease on record (Archives de méd. et de pharm. mil., 1888, xi, 481). Thayer, in 1902, was able to find but 9 cases in the literature, to which he added 1 of his own.

Symptoms.—There is an acute onset, usually without prodromal symptoms, but attended with fever, pain in the extremities, and swelling of the muscles. The muscles of the lower extremities are generally affected first, and in common with those involved later are hard and very tender upon manipulation. Starting in a single muscle or group of muscles, the condition spreads and may ultimately involve almost the entire voluntary muscle system. Owing to the severity of the pain and tenderness, voluntary movements of the extremities are greatly restricted. Edema of the subcutaneous tissues may be present and the skin becomes hyperemic, often purpuric, or even hemorrhagic. Later it becomes discolored or pigmented as the eruption disappears. Muscle atrophy is a rare sequel.

The myocardium is invariably affected, this leading to a wide range of circulatory symptoms varying from cardiac palpitation to dilatation, and not infrequently death results from cardiac failure. Bleeding from mucous membranes is not infrequent. Unlike dermatomyositis, the condition is generally not associated with enlargement of the spleen. Nephritis

is frequent, albumin and casts being found in the urine.

Diagnosis.—The following points should be remembered: The acute onset with fever, a hemorrhagic or purpuric skin eruption, and marked circulatory symptoms from the myocarditis.

Pathology.—Macroscopically the muscles, including the myocardium, are reddish brown in color, and contain numerous hemorrhagic foci. Microscopically, intramuscular hemorrhages are found between the muscle fibers, the latter in many instances having lost their nuclei and undergone vacuolation and degeneration. In the chronic cases there is a marked increase of connective tissue and more or less atrophy of the muscle fibers, and the presence of blood-pigment is noted.

Etiology.—The cause of myositis hemorrhagica is still undetermined, but is thought to be some form of infection. The disease has been known to follow sore throat and cervical cellulitis each in one instance, and in 2 cases staphylococci were obtained.

Prognosis.—The prognosis is grave, a majority of the cases terminating fatally.

Treatment.—The same measures are indicated as in dermatomyositis.

MYOSITIS FIBROSA.—Definition.—A rare disease characterized by inflammation of one or more muscles, which later become replaced more or less completely by fibrous tissue. The disease is of unknown origin, and runs a subacute or chronic course.

History.—Recognition of the disease dates from the report of a case by Gies in 1878 (*Deut. Zeit. f. Chir.*, 1879, xi, 161). Since that time but few cases have been recorded.

Symptoms.—The onset is gradual, beginning usually in the lower extremities. The disease progresses slowly and affects in turn different muscles or muscle groups. In one instance the disease was first manifest in the sternomastoid muscle (Janicke). Spontaneous pain may be a prominent symptom, but was absent in one case seen by Batten. The muscles are not especially painful upon palpation. Fever is absent. As the condition advances, contractures develop, the flexors of the extremities being chiefly implicated. The back becomes curved and the head flexed on the chest, the patient becoming ultimately rigid and helpless.

Muscular response to the faradic current is diminished or absent. Reactions of degeneration have not been reported. Sensation is, as a rule, unaffected.

Diagnosis.—It is difficult to separate myositis fibrosa from other forms of myositis. The diagnosis should be based chiefly upon the histological examination of a piece of muscle. In the other forms of myositis there is usually severe pain upon palpation of the affected muscle. This is slight or absent in myositis fibrosa.

The rigidity and contractures of cerebral diplegia present a superficial resemblance, but the signs of upper motor segment disease, such as increased reflexes, ankle clonus, and Babinski's sign, at once afford information of the true nature of the condition.

Myopathy could hardly be mistaken for myositis fibrosa unless contractures were marked.

Pathology.—The main feature is increase of connective tissue at the expense of the muscle fibers. The muscles are hard and firm and may be

swollen, presenting a tumor-like appearance.

In other cases the muscles are smaller than normal, but still hard and fibrous. Edema of the overlying tissues may be present.

On section the muscles present the white appearance of fibrous tissue, with reddish-yellow spots showing as the remains of the muscle fibers.

Microscopically, the muscle fibers show atrophy and granular degeneration, with disappearance of the cross-striations. Tendinous tissue appears to be increased, but, as Batten suggests, this may be only relative, resulting from the shortening of the muscles.

Etiology.—There has been much speculation as to the cause of myositis fibrosa. It has been variously considered as being of rheumatic origin, as a chronic form of primary non-suppurative myositis (Kader), as being related to osteomyelitis (Hackenbruch), and as belonging to the abiotrophies. Although the condition has been thought by some to be postinfectious, no micro-organisms have as yet been obtained in these cases. Trauma and syphilis seem to have no connection with the condition. It begins, usually, in early life.

Prognosis.—As a rule, the disease is steadily progressive, but instances of recovery have been reported. Improvement is always a probability, and the disease may be arrested and remain stationary.

Treatment.—**Massage, passive movements, electricity, and hot-air baths** are advocated early in the disease, and recovery has followed their use in some instances. Drugs have so far proved valueless. Batten has

suggested the use of injections of **thiosinamine** (fibrolysin) on theoretical grounds, but, so far as I can learn, these have not been tried.

MYOSITIS OSSIFICANS PROGRESSIVA.

DEFINITION.—A chronic, progressive, inflammatory condition, of unknown origin, characterized by the formation of osseous tissue in the muscles, tendons, fascia, and ligaments, with outgrowths from the bony skeleton.

Records of a small number of instances of progressive ossification of the muscular system have accumulated during the last century and a half and several medical museums contain skeletons in which massive bands of bone occupying the site of muscles are attached to the vertebræ, ribs, or pelvis and often rigidly unite them to the bones of the arm or thigh. Other instances of ossification, usually beginning during the first years of life and slowly implicating one muscle or group of muscles after another, have been described. Many of those affected show an anomaly of the great toes and in some instances of the thumbs. Both great toes are of small size, not extending beyond the first interphalangeal joint of the second toe. Opie (*Jour. Med. Research*, xxxvi, 267, 1917).

SYMPTOMS.—The onset of the disease is slow, the first symptom being a local swelling, usually painful, in some part of the muscular system, generally appearing first on the back of the neck. The muscle or muscles affected are indurated, the overlying subcutaneous tissues are edematous, and the skin slightly reddened or unaffected. Accompanying these phenomena, as a rule, is a slight rise of temperature. In a few days the swelling diminishes, but the muscle remains more or less indurated.

Then there is usually a quiescent period of a few weeks or even months' duration, followed by the occurrence of another attack. A series of these recurring attacks is the characteristic feature of the earlier stage of the disease. The majority of the muscular swellings ultimately become bone, some only reach the fibrous stage, while in a few the swelling disappears, leaving an atrophied muscle. In rare instances the swelling subsides and the muscle, instead of undergoing degenerative change, returns to normal.

In Lorenz's group of cases the disease commenced in the muscles of the back and neck in 21 out of 38 instances; in 7 it began in the shoulder muscles; the onset of the rest was distributed between the face and the upper and lower extremities. The affected muscles become ossified in from three to eight months, the process being usually painless, but causing rigidity and fixation of position. On account of the early implication of the muscles of the back of the neck and of the ligaments in the same region, the head is held forward or to one side. Later, as the ligaments and tendons become ossified and bony outgrowths appear from the skeleton itself, the shoulder-blades become bound to the back and the arms can be moved but little, being usually fixed in a flexed position at the elbows. The muscles of the back become attached to the skeleton, the spinous processes form a continuous bony column, and the back becomes rigid. The lower extremities are involved later and to a less extent, but the hips and knees may ultimately become locked in the same manner as the joints of the upper

extremities. Implication of the masseter, temporal, and pterygoid muscles not only prevents mastication of food, but may fix the jaw so as to make even the introduction of liquids through the mouth a matter of considerable difficulty.

The eye muscles are usually unaffected, but have been involved in rare instances. The muscles that escape are the muscles of facial expression, the tongue, the muscles of deglutition, the diaphragm, the perineal muscles, the muscles of the genital apparatus, and the sphincters. The hands and feet are practically always exempt.

Response of the muscles to the faradic current is either normal, diminished, or lost, and in rare instances reactions of degeneration have been found.

The skin and subcutaneous tissues overlying the affected muscles may slough from pressure and irritation, ulcers forming and rendering the patient liable to septic infection.

The establishment of the menstrual function is apt to be much delayed if the disease occurs in girls before puberty, and the menses are usually arrested if the malady occurs after this function has made its appearance.

A striking feature of the disorder and one which lends support to the theory of its resulting in part from a congenital defect is its association with congenital deformities, of which microdactyly is the most common, occurring in three-fourths of the cases. This peculiar condition was first described by Gerber and later emphasized by Helferich. The great toes and the thumbs are shorter than normal, because of a shortening of the phalanges, which, being united by a

bony ankylosis, gave the impression of an absent proximal phalanx until the X-ray revealed the true character of the deformity. The great toe is not as long as the second toe, and often points outward and sometimes under the adjoining toe. In the hands the shortening is not always limited to the thumbs, a corresponding defect of growth being sometimes observed in association with this in the little fingers. Among other malformations that have been noted are sexual infantilism; atrophy of the mammae, testicles, and scrotum; absence of certain muscles, and absence of the upper incisor teeth. Sympton (Brit. Med. Jour., ii, 1886, p. 1026) reported the interesting and much-quoted finding of microdactyly occurring in the father of a case of myositis ossificans, although the man had no evidence of the muscle disease.

According to Sidney Lange, the X-ray picture of the stage of ossification is characteristic, and it is described by him as follows: "Osseous masses, usually elongated or ribbon-shaped bands at first, are seen among the muscle fibers and running parallel to them. These masses branch in irregular fashion and take on irregular and grotesque shapes. Although they are believed to originate primarily in the muscles, some of the masses may be seen adherent to and apparently an outgrowth of the neighboring periosteum and bone."

In traumatic cases, the X-ray may soon show a faint, irregular shadow with light and dark areas (Gruca).

DIAGNOSIS.—Early cases are frequently considered as rheumatic or the result of trauma. After the disease has progressed, however, its symptoms are so distinctive that they

could hardly be mistaken for any other condition.

Multiple exostoses occur at the diaphyses and epiphyses, and in this condition the muscles are not primarily affected.

As has been pointed out by Coley, myositis ossificans developing in a young adult shortly after an injury would present a history almost identical with that observed in sarcoma. In myositis ossificans pain in the early stages is marked, while in sarcoma it is usually absent. In the former condition increase in size of the tumor, if present, would be slight, while in the latter affection there would be a steady and fairly rapid enlargement. Palpation would reveal a difference in consistency of the tumors, that of myositis being harder than that of sarcoma.

In periostitis and osteomyelitis the pain is more severe and worse at night, and the muscles, as in the case of multiple exostoses, are not affected primarily.

Other conditions which have a superficial resemblance to myositis ossificans are spondylitis deformans, the Charcot joints in tabes, and muscular dystrophy.

PATHOLOGY.—In the early stage of the disease the intramuscular connective tissue becomes infiltrated, chiefly in the vicinity of the blood-vessels, with embryonic connective tissue, which proliferates and later develops into adult fibrous tissue. This contracts, with consequent induration of the connective-tissue mass and secondary atrophy of the muscle fibers. In the final stage the connective tissue undergoes ossification. Macroscopically, in the first stage the muscles implicated are

yellowish red in color, soft, and swollen. In the second stage the muscle becomes lighter in color, with reddish streaks representing the remaining muscle fibers, and has the consistency of a fibroma. In the terminal stage the mass takes on the hardness of bone.

Under the microscope, the muscle fibers show secondary atrophy and fatty and granular degenerative changes, with a few normal fibers remaining at the periphery. The cross-striations disappear and the sarcolemma nuclei are markedly increased. The process of ossification begins in the connective tissue between the muscle fibers, toward the center of which are seen small spaces containing the so-called "formative cells," which subsequently become osteoblasts and bone-corpuscles. These primary bony foci enlarge and later unite to form larger osseous masses which resemble true bone in every particular. Elliott, reporting a typical case, concluded that there was "no doubt that myositis ossificans progressiva is an inflammatory progressive myositis." His opinion as to the nature of the process, however, was based on the clinical course of the disease and is not confirmed by the pathological findings. Goto, in another pathological study, concluded that the malady is not inflammatory nor of a neoplastic nature, but due to a congenital defect in the differentiation of the connective-tissue elements. Helferich describes the cause as an inferiority of the mesenchyma. That the calcium metabolism is normal has been shown by the investigations of Austin on a patient of Painter's.

Hoag and Soletsky observed a case of *creaking in the muscles*, and found 3 cases

recorded in the literature. In their case, a piece of muscle was removed from the left scapular region, where the crepitus was most marked. The findings were localized thickenings in the aponeurosis and muscle, which had been caused by hyaline swellings. The cause of this affection is over-exertion, resulting in small areas of rupture in the muscle and the aponeurosis, followed by minute hemorrhages and hyaline thickenings, which cause a creaking when the two surfaces rub together.

ETIOLOGY.—The theories that have been advanced as to the origin of myositis ossificans are numerous and interesting. It has been considered as being of a rheumatic nature (Stonham), as a new growth (Mays, Ziegler), a trophoneurosis (Nicoladoni, Kleen, Eichhorst), and a form of atavism (Brennshon). Maunz has suggested that there is an embryonic displacement of the bone nuclei within the muscle substance. Another view, strongly advocated by Rolleston and by Elliott, is that two factors are concerned: a congenital deficiency in the resisting power of the muscles which renders them susceptible to inflammation from what would ordinarily be inadequate exciting causes, and a morbid predisposition to aberrant bony formation.

Of exciting causes, trauma is the only one that stands out at all conspicuously, although exposure to cold has been mentioned as a possible factor in some instances. Many cases develop without any apparent exciting cause.

Myositis ossificans is not uncommon among mounted troops. Probably both a diathesis and an exciting cause are necessary in its production. In diagnosis the main problem is to rule out sarcoma. Generally the X-ray will decide; if not, an exploratory incision is permissible. In both of the writer's cases a rider had sustained severe

strains of the thigh muscles in putting a horse through fence jumping. In the first case within 5 weeks and in the second within 6 months, a lump developed between the pubis and Poupert's ligament, growing into a hard, bone-like mass. The X-ray showed that the bony masses were not connected with the skeleton. Operation was not considered necessary. A. Bowen (Arch. of Surg., Nov., 1924).

The condition may follow either closed or open trauma. Jones and Morgan, in 339 cases, found the order of frequency as follows: Brachialis anticus, quadriceps, adductor longus, and biceps. Other muscles reported involved are: Gluteals, temporal, masseter, thumb muscles, pectoralis major, deltoid, triceps, quadratus femoris, soleus, tensor fasciæ femoris, tibialis anticus, forearm muscles, coracobrachialis, and sternomastoid. In the quadriceps the condition generally arises from a blow on the football field; in the brachialis anticus, from a posterior dislocation or intra-articular fracture of the elbow. In 3 to 4 weeks an X-ray shadow is apparent, separated from the diaphysis by a zone of light. The tendency is eventually toward a certain degree of reabsorption. In many cases perfect function has been restored. T. P. Noble (Surg., Gyn. and Obstet., Dec., 1924).

The great majority of the cases of myositis ossificans are first observed before puberty, and the largest number of these during the first few years of life. The malady has developed as late as 35 years (Rogers) and 54 years (Kroncker), and as early as the fifth month (Garrod).

Males are affected more frequently than females, the ratio being about 4 to 1. According to Steiner, the disease begins earlier in women.

Germany and England appear to furnish the largest number of the cases, although the malady is not anywhere common.

PROGNOSIS.—The disease is chronic and progressive, with intermissions, varying from a few weeks to many years' duration, in which actual improvement may occur, only to be eventually followed by relapse. The bony tumors remain undiminished once they are established. Death may result from pyemia due to infection from bedsores, from tuberculosis, or from pneumonia or other intercurrent affection.

TREATMENT.—It should be remembered that the acute attacks or exacerbations may result from trivial causes, as a slight blow or exposure; much care should, therefore, be taken to avoid such occurrences.

Medical treatment, including organotherapy, has proved valueless.

Excision has been tried, but is followed by recurrence.

In the traumatic cases the treatment in the early stages is **rest** and **fixation**. When the process has ceased and begun to consolidate, **massage** and **exercise** are called for (Makins). **Excision** is only to be considered after 6 months and if distinct functional disability exists or a large vessel or nerve is interfered with. T. P. Noble (Surg., Gyn. and Obst., Dec., 1924).

Case of a boy of 2 years with progressive ossifying myositis in which the disorder was vastly improved by a **diet** causing artificial acidosis, *viz.*, 30 to 40 Gm. of proteins, 30 Gm. of carbohydrates and up to 140 Gm. of fat daily. T. Frölich (Acta ped., Mar. 6, 1926).

When fixation of the jaws occurs, it is sometimes necessary to **remove teeth** to facilitate feeding.

MYASTHENIA GRAVIS.

SYNONYMS.—Bulbar paralysis without pathological lesions; asthenic bulbar paralysis; pseudoparalysis myasthenica; Erb's disease.

DEFINITION.—A disease characterized clinically by motor impairment, chiefly glossopharyngolabial, varying in degree from slight exhaustibility to complete paralysis, and pathologically by the absence of definite lesions in the nervous system and the presence of lymphocytic infiltration (lymphorrhages) in the muscles.

HISTORY.—Although myasthenia gravis is sometimes spoken of as Erb's disease, from his description in 1878 of cases presenting a bulbar syndrome, yet differing in course from chronic progressive bulbar paralysis, cases of the disease had previously been reported by other writers. Wilkes, in 1877, recorded a case, but without much elaboration. Willis and Bazire had also reported cases. It remained for Oppenheim, in 1887, to direct attention to and stimulate interest in the disease by an elaborate description, with detailed microscopical study, of a case he had observed clinically for some time. Goldflam emphasized the occurrence of oculomotor paresis and called attention to the rapid exhaustibility of muscles upon voluntary effort, while Kuh and Braude (*Jour. of Nervous and Mental Dis.*, Oct., 1913, x1, No. 10) subsequently observed in a case reported by them that a feeling of fatigue was produced by passive movements. Jolly, in 1895, studied the reaction of the muscles to faradic currents and found that with repeated electrical stimuli the muscular contractions would become successively weaker, but would regain their former excitability after a brief rest. He termed this phenomenon the "myasthenic reaction." Buzard observed that muscles fatigued by the faradic current still retained their excitability for the galvanic current. Weigert was the first to describe the lymphatic muscular infiltration which has since been confirmed by numerous observers.

SYMPTOMS.—As the name indicates, muscular weakness is the chief feature of the disease. This varies from slight exhaustibility to complete paralysis, and affects the skeletal muscles in general and those supplied by

the motor nuclei in the bulb in particular. Not only does this fatigability vary in different muscles in a given case, but from time to time in the same muscles. Volitional movements or electrical stimuli cause first exhaustion, then, if continued, paresis. After an interval of rest the muscle response is again normal.

The onset of myasthenia is usually gradual, but may be more abrupt. In the latter case there may be an accompanying general malaise with headache. Oculomotor weakness is a common initial symptom, ptosis being perhaps the most frequent. Next in frequency is involvement of the muscles of mastication, articulation, and deglutition. The disease may remain limited to these muscles or even to the oculomotor group, or less frequently, or in advanced cases, the muscles of the trunk and extremities may also be implicated. Starr, however, noted that in one-third of the cases the weakness was first felt in the arms or legs.

A short walk may so tire the patient as to compel him to sit down. The tiring of the muscles of the mouth, throat, tongue and larynx is strikingly manifested in the reduction of the tone of voice as the patient continues to talk, until it may give out altogether. The disease may announce itself first by tiring of the legs, by ptosis, or by difficulty in deglutition. There is no atrophy or fibrillary twitching, no pain or other sensory changes, and the mental state remains normal. The patient often awakens in the morning, after a refreshing sleep, apparently entirely free from all symptoms. Attention has been called to a large, persistent thymus gland, and in 1 of the author's cases the autopsy revealed such a thymus with fatty degeneration. Several observers have noted a lack of calcium in the body, and this finding

was confirmed in 1 of the writer's cases. The mortality from this disease may be estimated at at least 50 per cent. Some cases improve and finally recover. Other cases apparently recover, and then fall into a fatal relapse. T. Diller (*Atlantic Med. Jour.*, June, 1925).

The first symptom may be a drooping of the lids, appearing toward evening, and disappearing after the night's rest; as the disease progresses, some ptosis may remain even in the morning. Next, varying degrees of strabismus may make their appearance.

While the affection is usually bilateral, corresponding muscles may not be affected to the same extent. Thus one lid may droop more than its fellow, and the eyeballs may be on different planes. The irregular involvement of the ocular muscles may cause nystagmoid movements upon volitional motion of the globes. When the ptosis is marked the patient either uses his occipitofrontalis or holds his head backward in the effort to overcome the resulting difficulty in seeing. Loss of the pupillary light reflex is rare, but it is not uncommon for the iris to show exhaustion if the test is repeated. Reaction to accommodation is apt to show the characteristic exhaustion, but it may not be affected.

Of the facial muscles, the orbicularis palpebrarum is the most likely to escape. Implication of the other facial muscles causes loss of expression, drooping of the corners of the mouth, inability to whistle or blow out a lighted candle, and drooling of saliva. Difficulty in masticating and in articulating result if the muscles governing the lower jaw are affected. Difficulty in swallowing, with regurgitation of fluids through the nose, results from paralysis of the muscles of

the palate, and if the tongue is involved there is added difficulty of articulation and food is not properly removed from the mouth. From paresis of the laryngeal muscles aphonia may result.

It must be remembered that all the conditions described above may be manifest in varying degrees of intensity or severity, according to the degree of fatigability of the muscles present.

Weakness of the muscles of the neck causes difficulty in holding the head upright, patients so affected frequently using their hands as an added support. Involvement of the truncal muscles may be so extensive as to confine the patient to bed; but the chief danger results through implication of the muscles of respiration, with dyspnea and a possible fatal termination from suffocation.

The muscles of the extremities are not, as a rule, involved to the same extent as those of the face and neck. They may be affected at any stage of the disease, the proximal muscles being more frequently implicated than those more distally located. Through involvement of the muscles of the hand, writing may show the characteristic fatigue, and when the muscles of the lower extremities are affected walking obviously becomes difficult. A sudden "giving way" of the legs may be an early symptom.

All of these manifestations are apt to be slight after the night's rest, becoming progressively worse toward evening.

Conditions affecting the general exhaustibility are emotion, exposure to extremes of temperature, menstruation, and exertion, whether local or general.

Myasthenic Reaction.—The reaction of the affected muscles to electrical stimulation is characterized by the following phenomena: There is a gradual diminution in the muscular response to faradic shocks of a given strength, from strong contraction at first to complete failure to respond after repeated stimulation. After a brief rest the original strength of reaction returns, only to diminish progressively again, and more rapidly than before, in response to further stimulation.

Muscular reaction to the galvanic current is unchanged or but slightly diminished in myasthenia. An interesting phenomenon, however, is that after a muscle is exhausted by and fails to respond to the faradic current it will still react to the galvanic current (Murri) and to voluntary effort.

In muscles that have actually undergone atrophy, the reaction of degeneration has been observed (Buzzard).

Tendon Reflexes.—These are preserved even when the corresponding muscles are exhausted, but may be diminished in advanced cases. Ankle clonus and Babinski's sign are absent, irritation of the sole of the foot being followed by the normal flexion of the great toe.

Sensation.—In an uncomplicated case of myasthenia sensory disturbances are absent or limited to paresthesiæ, or an aching or slight pain in the extremities.

Sphincters.—The functions of the bladder and bowels are, as a rule, unaffected, although in rare instances slight urinary incontinence has been observed.

Psychic Symptoms.—It may be said that in myasthenia the mind is un-

affected, although cases have been reported in which there has been a coincident melancholia.

Urine.—A diminution in the amount of creatinin excreted has been observed (Spriggs), while the amount of uric acid eliminated is unchanged.

DIAGNOSIS.—While the infrequency of myasthenia gravis may cause it to be overlooked, the purely motor character of the disease which affects primarily and chiefly the muscles supplied by the bulbar nuclei, the characteristic exhaustion without paralysis in the affected muscles, the myasthenic electrical reaction, and the absence of fibrillation, atrophy, and the reactions of degeneration form a combination that should offer no difficulty in recognition if borne in mind.

In chronic polioencephalitis there is distinct muscular wasting, with reactions of degeneration, or at least diminished response to electrical stimuli. There is also fibrillation, and the course is not marked by remissions.

Pseudobulbar palsy gives a history of two or more apoplectic attacks; the upper part of the face is uninvolved, and signs of upper motor segment lesion are present.

Multiple neuritis in general and diphtheritic paralysis in particular offer a superficial resemblance, but there is a definite history of cause and onset and a different response to electrical tests.

In advanced cases of neurasthenia the exhaustion is marked, but neurasthenics are notoriously worse in the morning and at their best in the evening.

Hysteria may present the same irregular remissions and exacerbations in its course, but hysterical

palsies of the face are rare, and the associated sensory "stigmata" of hysteria are usually conspicuous.

The resemblance of certain cases of muscular dystrophy to myasthenia has been commented upon by Gowers, Oppenheim, and others, but in the former affection there are marked muscular atrophy, an absence of the myasthenic reaction, and an absence of involvement of the muscles of deglutition.

In a case of myasthenia gravis with progressive atrophy involving especially the muscles of mastication and of the face, the P and T peaks were lacking in the electrocardiogram. Direct mechanical irritability of the muscles was increased. As endocrin disturbances the patient showed, with the adynamia, lymphocytosis and lack of libido. Schäffer and Briger (Deut. Arch. f. klin. Med., Dec. 20, 1921).

PATHOLOGY.—The most constant and characteristic finding in myasthenia gravis is an infiltration of small round mononuclear cells (lymphocytes), chiefly in the muscles, but also in other tissues and organs.

Since Weigert's original observation of this condition in 1901 (Laquer and Weigert: Neurol. Centralbl., 1901, xx, 595) the finding has been repeatedly verified. Knoblauch in 1908 found the "lymphorrhages," as they were termed by Buzzard, in portions of muscle studied *ante mortem* from a case of myasthenia gravis.

The cellular accumulations vary in size from the smallest possible number to collections large enough to be distinguished by the naked eye in a stained section (Buzzard). They are found between the muscle fibers, which in rare instances are involved by the cells. Some observers have found slight degenerative changes in

the muscle fibers thus involved, but everywhere else the fibers are, as a rule, unchanged. A serous exudate and minute capillary hemorrhages have also been seen. In the larger collections of cells a delicate reticulum is found, giving an appearance closely resembling lymphoid tissue. Slight muscular atrophy is an exceptional finding.

In the nervous system lymphorrhages have been found in isolated instances in the posterior root ganglia of the cord and in the medulla. Kuh and Braude have reported the occurrence of an aberrant bundle of fibers in the cervical region of the cord, but this was probably an anomaly, comparable with the micrognathia, polydactyly, and doubling of the great toe observed in cases by Oppenheim and upon which he placed considerable importance as indicating a probable congenital predisposition, a view not held by most writers. Numerous minor findings have been recorded, such as recent hemorrhages, excess of glial tissue, capillary thrombi, and chromatolytic and pigmentary changes in nerve-cells; but these are not held to have any special significance. The striking feature of repeated examinations of the nervous system in myasthenia gravis by competent observers has been the universal absence of any characteristic lesion.

Next in frequency to the muscular system, morbid changes have been found in the thymus gland. Buzzard divides these conditions into three classes: (1) Simple hypertrophy, where the gland has not undergone the usual regressive changes; (2) hypertrophy with degenerative and proliferative changes, and (3) new

growth, including such conditions as lymphosarcoma and lymphangioma. It must be remembered, however, that the majority of cases present no thymus abnormalities.

Lymphorrhages have been found in the thyroid gland, adrenals, liver, and pancreas, and in one instance (Tilney) there was an adenoma of the hypophysis.

Moderate lymphocytosis of the cerebrospinal fluid has been observed. The urine and blood have been examined with negative results.

When the data regarding the pathogenesis of any disease are meager, hypotheses are numerous, and myasthenia gravis is no exception to this rule.

The disease has been variously considered as a neurosis (Oppenheim), as due to faulty hepatic metabolism (Kauffmann), and as the result of hyperparathyroidism (Chvostek). Buzzard suggested that an unequal functional activity of the muscle elements, that of the sarcoplasmic fibers being diminished, could result in the rapid exhaustion of the red muscular fibers. Knoblauch advocates the theory that there is an increase of the pale and a diminution of the red fibers. McCarthy cites the work of Botazzi and Joteyko and their contention that in muscles there are two contractile substances, a fibrillar and a protoplasmic, which respond differently to electrical stimuli, and offers the theory of a selective poison reducing the excitability of the protoplasmic element.

That some toxin as yet undiscovered is responsible for the curious clinical manifestations of myasthenia is the general belief. The idea of an exogenous toxin is advocated by some on account of the numerous instances

recorded in which myasthenia has followed an acute infection. The weight of evidence, however, seems to favor an endogenous toxin resulting from a defect of internal secretion.

Stress laid on an inverted vasomotor reaction, consisting in dilatation of the vessels during voluntary muscular contractions in myasthenia. The cause of the inverted reaction seems to be a reduced formation of substances that control vascular tone. This disturbance probably affects the acid-base balance of the muscle fibers, stimulating the activity of the hydrolytic and lipolytic ferments and thus creating disorder in the muscles. The writer ascribes his 2 cases to disturbances of the vegetative nervous system of adrenal origin. In a patient who improved remarkably under *adrenalin* the inverted vasomotor reaction was absent, while it was present in the other case, which still had marked muscular weakness. Changes in the adrenals may also lead to parathyroid overactivity, with resulting hypercalcemia. G. Marinesco (Bull. Soc. méd. des hôp. de Paris, Nov. 6, 1925).

ETIOLOGY.—Myasthenia gravis occurs in the two sexes with nearly equal frequency, females slightly predominating. The majority of cases occur in the third and fourth decades, although cases have been reported under 10 and over 60 years. McCarthy has shown that in women the disease appears at an average earlier age than in men.

The disease is neither hereditary nor familial. Indirect neuropathic heredity also seems to play an unimportant rôle. Oppenheim emphasizes a congenital predisposition and cites a list of congenital anomalies that have been observed in his own and other reported cases.

The onset of myasthenia gravis has followed acute infectious diseases in

a considerable percentage of cases, influenza being the most frequent. Other preceding infections have been typhoid fever, diphtheria, scarlet fever, puerperal infection, and syphilis. There is nothing to indicate a direct relationship between myasthenia gravis and syphilis, tuberculosis, or alcoholism.

Numerous observers have recorded cases of myasthenia gravis in association with exophthalmic goiter, but, while this relationship is certainly more than coincidental, its significance is as yet unexplained. In isolated instances the disease has been found associated with Banti's disease (S. Mohr) and with angioneurotic edema (Diller).

Pregnancy, lactation, and menstruation usually have a deleterious effect on myasthenia gravis, although there have been exceptions to this rule, notably in a case reported by Goldflam.

When so many and so varied conditions are mentioned in connection with the etiology of a disease it is obviously difficult to select any one as being of chief importance, and to add still further to the obscurity Gowers reported a case of myasthenia gravis occurring after poisoning by petrol fumes, and Buzzard one following poisoning from coal gas.

PROGNOSIS.—Myasthenia gravis is a serious and uncertain affliction. It may run an acute course and terminate fatally in a few weeks, or may last for years. Some few cases recover; remissions are of common occurrence, and fatal termination is frequent.

TREATMENT.—In the treatment of myasthenia the first consideration is the avoidance, as far as possible, of

factors known to aggravate the condition. The patient should have **rest** and **quiet**, preferably in bed, and should be **kept warm**. The **food** should contain a **maximum** of **nourishment** and **require** a **minimum** amount of **mastication**. Feeding by the stomach-tube is not to be advocated unless deglutition becomes extremely difficult, as the act of passing the tube is accompanied by both emotional excitement and muscular effort in the attempt by the patient to swallow the tube. This is pointed out by Oppenheim, who mentions a case that died from suffocation during an attempted artificial feeding.

Electrical stimulation of the muscles by the faradic or galvanic current is contraindicated. **Central galvanization** is recommended by some, but the most that can be said of this form of treatment is that it does not seem to have caused any harm. **Massage**, if used at all, must be practised carefully, as it is capable of doing harm.

Extracts of the various **ductless glands** have been used, sometimes with favorable results. Marinesco recommends injections of **adrenalin**, subcutaneous, intramuscular or intravenous.

Arsenic, **iron**, and **strychnine** may be used, chiefly in the hope of improving the patient's general condition.

The administration of **calcium** has been advocated by Pemberton and by Diller.

Considerable improvement followed exhibition of 5 Gm. (75 grains) of **thymus extract** thrice daily. A. McLane Hamilton (Jour. Amer. Med. Assoc., May 25, 1912).

Pituitary extract, combined with **ovarian**, found useful in 2 cases. Lagane (Presse méd.; Charlotte Med. Jour., Nov., 1913).

Stress laid on **timing deglutitions** while eating, to give the muscles a short respite, *e.g.*, 2 to 4 minutes. The food should be easily masticated. The patient should drink from a spoon. Monrad-Krohn (*Norsk Mag. f. Laeg.*, May, 1918).

Case markedly improved for 5 months under **extract of whole adrenals**. It was particularly useful for the dyspnea and difficulty in swallowing. The patient later died, however, of pulmonary edema. Marked lesions of the adrenals were found. Pierre Marie, Bouttier and Bertrand (*Ann. de méd.*, Sept., 1921).

Four patients recovered, 2 became practically well, and 4 improved out of 14 cases seen in 25 years. **Strychnine sulphate** in large doses was used. One patient was given 92 hypodermic injections of $\frac{1}{4}$ grain (0.009 Gm.) twice daily, followed by $\frac{1}{12}$ grain (0.005 Gm.) doses twice daily. He remained well for 1 year, dying then of cancer. Another case was given ascending doses up to $\frac{1}{6}$ grain (0.012 Gm.) twice daily at the fourth week. In 2 or 3 months he was back at work, and had remained well 10 years. Dana (*Jour. Amer. Med. Assoc.*, Jan. 28, 1922).

MYOTONIA CONGENITA.

SYNONYM.—Thomsen's disease.

DEFINITION.—A congenital disease the chief feature of which is an interference with voluntary movement by reason of stiffness of the muscles.

HISTORY.—The first detailed description of this disease is ascribed to Thomsen, a Danish physician, in 1876. Thomsen was himself a victim of the malady, which had appeared over twenty times in four generations of his family.

SYMPTOMS.—When the patient attempts to make a voluntary movement, the muscle groups involved go into a state of tonic contraction. This retards the intended movement for some seconds; then the muscles relax slowly until the movement can be consummated. With repetitions

of the movement, each successive effort is performed more easily, the stiffness gradually disappearing until the movements are made without difficulty. After an interval of rest, the spasm reappears when the movement is again attempted.

Excellent examples of this curious phenomenon are seen in sudden attempts of the patient to clench the fist or to walk. In advanced cases, upon a sudden attempt at movement when the patient has been quiet or, as mentioned by White (Allbutt and Rolleston, "System of Medicine," vol. vii, p. 27), if he trips against a stone while walking, he may fall and be rigid and helpless until the muscles gradually relax.

The malady usually involves the majority of the voluntary muscles to some extent, but this involvement may vary greatly in intensity in different parts of the body. It is not uncommon to find the upper or lower extremities profoundly affected and the face undisturbed. Next in frequency and extent to the involvement of the extremities is that of the truncal muscles. The muscles of the head and neck are frequently affected, those of the face less often. The ocular muscles are sometimes implicated; likewise the tongue. Oppenheim cited a case in which the orbicularis palpebrarum alone was distinctly affected. The pharyngeal and laryngeal muscles are among those least apt to be involved, and the respiratory muscles are also rarely implicated. Swallowing and respiration therefore are not affected, and the same is true of the acts of micturition, defecation, and parturition.

The affected muscles are large, well developed, sometimes enormous,

but notwithstanding their large size the actual strength, as shown by the dynamometer, is, as a rule, subnormal.

General fatigue and emotion appear to aggravate the condition, which is also more marked after a long rest. **Warmth** and **mental rest** appear to exert a beneficial influence.

Electrical Reactions.—These have been termed by Erb the “myotonic reaction” (My R) and are as follows: The excitability of the nerves to the faradic current is normal, with the exception that a strong current causes a persistent tonic contraction of the muscle. When the galvanic current is applied to a muscle it responds promptly and about equally to both K. C. C. and A. C. C., the latter sometimes giving the stronger reaction. A characteristic feature is a slow, tonic contraction with reluctant relaxation, the contraction lasting several seconds when a strong current is applied. Application of the stable galvanic current causes a wave-like undulation of the muscle, the wave passing from the cathode toward the anode. This last reaction is not always easily obtained, requiring rather large electrodes and a strong current. Reaction of the muscles to the static spark is unaltered (Oppenheim).

The **mechanical excitability** of the muscles is not increased, but tapping the muscles will give the characteristic slow, tonic contraction, persisting for some seconds. There are no sensory changes and pain is absent, even during the tonic muscular contractions.

The **reflexes** are usually normal, but there may be a diminution of the knee-jerk. In rare instances this reflex has been lost. The blood-pressure has been found increased (Guillain).

An association of the disease with migraine and epilepsy is not uncommon, and mental symptoms have also been recorded as a complication of myotonia.

Association with other states has been frequent and the associated conditions numerous and varied, but with the exception of those mentioned and of myopathy (Charcot, Nonne) they do not seem to be of any importance.

The belief that progressive muscular atrophy may develop from myotonia is held by Hoffmann and other observers.

DIAGNOSIS.—The peculiar clinical picture presented by Thomsen's disease, together with the “myotonic reaction,” make the malady easy of recognition. *Myotonia acquisita*, described by Talma, presents an increased excitability of the muscles to electrical and mechanical stimuli, but is an acquired affection, transient and curable. The spasms come on chiefly after exertion and the muscular rigidity is retained to some extent after rest.

In Eulenberg's *paramyotonia congenita* the myotonic reaction is absent and the muscular spasms are induced by cold.

PATHOLOGY.—Microscopically changes are found in pieces of the muscles excised during life. The fibers show marked hypertrophy, being twice as large as normal, or even larger; there is an increase in the number of the sarcolemma nuclei and possibly a slight increase of the interstitial tissue. The cross-striations are not clearly defined. The same changes have been found *post mortem* (Dejerine and Soltas). Vacuolation has been observed, but it is not a constant finding. No pathological

changes have been found in the nervous system.

That the disease is congenital is well established by its occurring in several members of the same family, and the very early appearance of the symptoms strongly suggests an anomaly of development of the muscle fibers. The theory of a toxic origin has been suggested by the fact that corresponding symptoms have been produced by certain poisons (Joteyko, Bechterew).

ETIOLOGY.—No cause of the disease is as yet known. It appears usually in earliest childhood, but may remain latent until adolescence. It is more frequent in males than females (8 or 9 to 1). Fright has preceded the onset of the malady, but not to the extent that it can be given any value as an etiological factor.

Heredity plays an important rôle, the disease almost invariably appearing in several members of a family, brothers, sisters, parents, uncles, aunts, etc. While other neuroses and psychoses have appeared in the families of some of the reported cases, they are so commonly absent as to deprive their occurrence of any special significance. Consanguinity in the parents has been noted in some cases.

According to McCouch and Ludlum, there is evidence that thyro-parathyroid deficiency is etiologically related to myotonia congenita.

A large percentage of investigators of myotonia and paramyotonia have noted the coexistence of psychopathies and the myotonia in members of the same family. Sometimes they coexist in the same individual. This was the case in the first generation of the family described by the writer, while in the second generation there was a clear-cut separation of the two disorders,

each becoming associated with a definite physical type of person (3 cases in each instance). In the third generation the psychosis, as well as the physical type associated with it, was eliminated. Three of the total of 9 cases suffered no physical discomfort from the disease. In 1 the manifestations could be evoked only by strong psychic stimuli. The writer ascribes the condition to some inherited factor harmful to the neuromuscular apparatus. Where the musculature is not congenitally of large volume, the muscular system is spared, and the injurious agent acts on the highest cerebral structures, thus explaining the occurrence of psychoses and also that of transitory and acquired forms of the disease. J. Rosett (Brain, June, 1922).

PROGNOSIS.—The disease of itself is never fatal, but, once having made its appearance, the malady exists throughout the life of the individual. It shows no tendency to progress, neither does it disappear, although remissions may occur. According to White, the stiffness is somewhat more marked at puberty.

Myotonia atrophica, sometimes also known as *dystrophia myotonica*, is a disease which in many respects forms a link between Thomsen's disease and the familial muscular dystrophies. Its leading features, according to Batten's classic description, are as follows: A patient, usually a male, between the twentieth and thirtieth years of life, begins to complain of weakness of the limbs and wasting of muscles. Some stiffness of muscles may also be complained of. On examination he is found to have weakness and atrophy of the facial muscles, of the sternomastoids, of the flexors and extensors of the wrist, of the extensor of the leg or dorsiflexors of the foot, and the striking myotonic phenomenon that after grasping an object he has difficulty in relaxing his grasp. Pathologically there is a general cirrhotic condition of the muscles, such as is found in muscular dystrophy. The spinal cord may show some degeneration in the

posterior columns, but the other portions of the nervous system are normal. When once seen the condition is easy of recognition.

The fully developed myotonia atrophica is confined in the main to one generation, the members of the preceding generations, however, often developing cataract, which appears at an earlier age in succeeding generations. In the dystrophic generation itself some members remain healthy, some may have cataract alone, some may suffer from an incomplete form of the disease (absence of muscular atrophy), and others present both atrophy, myotonia and extramuscular symptoms. Adie and Greenfield (Brain, May, 1923).

TREATMENT.—Nothing is known that will cure myotonia congenita, and drugs avail nothing toward relief of the symptoms. **Systematic gymnastics**, as first advocated by Oppenheim, have proved of some value. Gessler's suggestion of stretching the nerves to produce atrophy of the muscles is only mentioned that it may be condemned.

DYSTONIA MUSCULORUM DEFORMANS.

SYNONYMS.—Dysbasia lordotica progressiva; torticollis; tonic torsion spasm.

DEFINITION.—A disorder featured by localized changes of tone in certain muscles or muscle-groups, with resulting clonic and tonic myospasms and varying grotesque deformities.

SYMPTOMS.—Previous to Oppenheim's description of the condition as a separate disease in 1911, most of these cases had been regarded as instances of Huntingdon's chorea, double athetosis, tic or hysteria.

The outstanding manifestation consists of wave-like, somewhat rhythmic, torsional movements, generally beginning in the upper limbs, but with their chief and ultimate seat in the muscles of locomotion. On standing and particularly in walking, curious deformities occur, some cases showing the "scissors gait," with the limbs crossed on account of hyperadduction of the thighs, others the "dromedary gait." The trunk is

thrown forward from the pelvis, producing a marked lordosis, and the lower limbs are thrown about awkwardly, the muscle-groups concerned being in alternate states of hyper- and hypotonicity. An attitude of the feet sometimes noted has been compared to a half-moon—"semilunar foot." Torticollis may also be present.

Voluntary movements, when performed, suggest a conflict of muscle-groups. Most of the deformities and myospasms disappear in recumbency, but many of the patients, in relaxing, assume some definite, unusual posture which seems to promote subsidence of the spasmodic movements. The movements cease almost entirely during sleep.

In a case in a male aged 32 years reported by Diller and Wright, in which there was conspicuous involvement of the neck, shoulders and upper limbs, the patient hooked his left arm behind his back, partly to fix the arm and partly to hide the movements. All movements, as is usual, were worse on standing, and occurred constantly on walking.

Dysarthria, explosive speech, and dysphagia have been reported.

This disease is unattended with paralysis, muscular atrophy, or altered reflexes or electrical responses. The sensory sphere and the mental processes are not involved.

DIAGNOSIS.—The essential feature which differentiates the condition from other kinds of spasm appears to lie, as maintained by Hunt, in an inability to harmonize the reciprocal activities of the agonistic and antagonistic groups of muscles in any movement, a seeming reversal of muscular tonus being manifested. Thus, when the patient is asked to extend the flexed wrist, this result is obtained only after a series of involuntary flexions to an angle not previously attained.

PATHOLOGY.—Though definite evidences of organic nervous disease were not found in Oppenheim's cases, he ascribed the disorders to fine pathological changes in the cortical cells controlling muscle tone, a dystonia, *i.e.*, a disturbance of the coördination of muscle tone, resulting. According to Hunt, disease of the corpus striatum is responsible. Flater has recorded a case offering clinical ground for the assertion that the cause is to be looked for in the lenticular nucleus. In an autopsied case,

Thomalla found necrosis of the putamen. Pollock has called attention to certain relationships of the condition to progressive lenticular degeneration (Wilson's disease), and favors a grouping together of these and certain other disturbances as disorders of the lenticular nucleus (*dystonia lenticularis*), the symptomatology depending upon the precise nature of the involvement of the corpus striatum.

ETIOLOGY.—The disease affects usually children between the ages of 8 and 14 years, but is sometimes met with in older persons, and does not necessarily set in in childhood. Females are affected more frequently than males. Rarely a familial relationship between cases has been noted.

Little is known of the predisposing or exciting causes, other than that while some cases can only be designated as idiopathic, others have been postencephalitic. Flater has reported a case with tremulous movements of the extremities, partly choreiform and partly resembling paralysis agitans.

PROGNOSIS.—While temporary improvement may occur, the condition in general is chronic and progressive. It is not, however, lethal *per se*, the patients eventually succumbing to an intercurrent disorder. Considerable periods at times separate involvements of different portions of the body. In a case alluded to by Keschner the condition was unilateral for 9 years.

TREATMENT.—No efficient form of treatment is known. Where the movements are so active as to be exhausting to the patient, **sedative drugs** may be administered, much as in severe chorea. Intrathecal injections of **magnesium sulphate** have been tried, with temporary improvement. The remainder of the treatment consists of **hygienic measures**.

PROGRESSIVE LENTICULAR DEGENERATION.

SYNONYMS.—Wilson's disease; hepatolenticular degeneration.

DEFINITION.—A disorder combining a bilateral progressive degeneration of the lenticular nuclei and hepatic cirrhosis, and featured clinically by tremor, rigidity of the limbs and face, dysphagia, dysarthria, and mental deterioration.

SYMPTOMS.—As with the preceding disorder, this disease is nervous rather

than muscular; the prominence of active motor symptoms, however, and the desirability of establishing in detail a contrast between these conditions and the true muscular disorders, would seem to warrant their consideration in this place.

Bilateral progressive lenticular degeneration was described as a separate entity in 1912 by S. A. K. Wilson. The tremor resembles that of paralysis agitans, and extends from the hands in early cases to the whole body in advanced cases. It is increased by voluntary movement. The condition of the muscles is one of increasing hypertonicity, leading to contractures, and these, in turn, to persistent deformities, especially of the distal portions of the extremities. Voluntary movements, including locomotion, become increasingly difficult. The face is mask-like, frequently with separation of the lips due to muscular contracture. The difficulties in speaking and swallowing, and any pain complained of, likewise arise through muscular contracture, and not through paralysis or sensory involvement.

The degree of mental disturbance is variable. The condition is featured by exaggeration of emotional responses, with childishness, sometimes causeless laughter, restlessness and euphoria. A condition resembling dementia may finally supervene.

Clonic convulsions may be observed, especially in the more advanced cases. The cirrhosis of the liver constantly associated with the disease rarely causes any symptoms of the hepatic type.

DIAGNOSIS.—The absence of evidences of pyramidal tract disorder at once excludes a large number of the recognized nervous syndromes, including pseudobulbar palsy, while the symptoms actually present, coupled with the age of the patient and the usual familial incidence of the disease, are sufficiently characteristic to make the diagnosis easy.

PATHOLOGY.—The lenticular nucleus regularly shows softening, increase of glial tissue, and in advanced cases, complete degeneration with cavity formation. The degenerative process is more marked in the putamen than in the globus pallidus. At times the caudate nucleus shows some involvement.

The liver is of reduced size and of a pro-

nounced hobnail type, with histological evidence of attempts at regeneration. The spleen may be enlarged, and changes in the thyroid gland have at times been noted.

ETIOLOGY.—The disease usually sets in toward the end of the second decade of life, but has been observed in infancy, as well as later in life. It is familial, though not hereditary. The degenerative process in the brain has been ascribed to toxic substances derived from the cirrhotic liver. Paul has suggested that some unknown metabolic toxin is responsible for both the hepatic and lenticular lesions.

The condition may strongly resemble the juvenile form of paralysis agitans and, like the latter, has in a number of instances been apparently reproduced as a sequel of epidemic encephalitis. In doubtful cases of this type, the familial tendency, the early dysphagia and dysarthria, and the mental phenomena in lenticular degeneration are of differential assistance.

McConnell and Spiller have called attention to cases of lenticular softening developing some days after apparent recovery from carbon monoxide poisoning. In these cases, however, the reflexes may be exaggerated and the Babinski positive.

PROGNOSIS.—This is uniformly fatal. The cases have been divided into acute and chronic forms, differing symptomatically only in that the former is attended with irregular fever. The duration is from a few months to a year in the more acute cases, and an average of 4 years in the chronic. There is little tendency to remissions. In a case reported by M. L. Graves (South. Med. Jour., Oct., 1922), however, the patient was 68 years of age when seen on account of a fractured arm, and had had some symptoms since childhood, more lately supplemented by rhythmic flexion and extension of the fingers and toes, with a coarse tremor; the disease is thought to have become arrested up to the age of 58, at which time further degeneration and hepatic cirrhosis set in.

TREATMENT.—No curative treatment being known, symptomatic measures seem alone possible. S. Paul has, however, reported a case in an infant, with icterus, in which the nervous symptoms improved greatly on a diet of Liebig's malt soup; this improvement was ascribed to quickening of

intestinal peristalsis and decreased absorption of toxins. A search for and elimination of all possible sources of toxic absorption would seem desirable.

AMYOTONIA CONGENITA.

SYNONYMS.—Oppenheim's disease; myatonia congenita.

DEFINITION.—A disease appearing in early childhood, characterized by a flaccid paralysis with diminished or lost tendon reflexes, but without reactions of degeneration or marked muscular wasting.

SYMPTOMS.—The most conspicuous feature is the striking flaccidity of the affected muscles manifested at birth or shortly thereafter. The lower extremities are always affected, sometimes the upper extremities, and less frequently the trunk. The muscles of the face and the diaphragm usually escape, while the ocular muscles and those of mastication and deglutition are not involved. Active movement is not entirely lost, but greatly restricted, and the child appears as if paralyzed. So great is the degree of hypotonia that the extremities may be moved about like flails, and when unsupported the child presents a kyphotic deformity, which disappears when the child is raised by the shoulders. Contractures may occur.

Reaction of the muscles to the faradic current is diminished or lost, but reaction to the galvanic current is normal. The tendon reflexes are invariably lost, but return as the patient improves. Sensation is not altered and the sphincters are unaffected. The mentality is normal.

The evidence seems to be in favor of the identity of amyotonia congenita and the *Werdnig-Hoffmann disease* or "infantile progressive spinal muscular atrophy with distinct hereditofamilial tendency." In the writer's case, aged

13 months, the spinal column appeared abnormally long. There was almost complete paralysis and loss of tone of all the skeletal muscles, especially the limb muscles. The child later died of bronchopneumonia. W. J. Close (Med. Jour. of Austral., Feb. 23, 1924).

DIAGNOSIS.—The early onset, the extreme flaccidity, and the absent tendon reflexes and characteristic electrical reactions should render the diagnosis a comparatively simple one.

Myopathy appears at a later period, occurs in definite muscle groups, is progressive, and shows distinct muscle atrophy. Amyotonia never progresses, but usually improves, and there is no family tendency.

Obstetrical palsies are generally unilateral; amyotonia is symmetrical.

Infantile paralysis gives the history of an acute onset, with usually some constitutional symptoms followed by abrupt loss of power in one or more of the extremities. The reactions of degeneration are usually present.

PATHOLOGY.—The muscles, while not visibly atrophied, are small and yellowish in color, and an unusual amount of fat is seen between the muscle bundles. Microscopically, the majority of the muscle fibers are much smaller than normal, while interspersed here and there between the smaller fibers are found fibers with a size greater than the normal. The small fibers may show a marked increase in the number of the sarcolemma nuclei, or may have only the usual number. The cross-striations are distinct, and there are no degenerative changes. The large fibers also show well-marked cross-striations and have the normal number of nuclei, but show distinct regressive changes, such as centric displacement of the nuclei, vacuolation, and longitudinal cleavage

of the fibers. In the affected muscles there is increase of connective tissue.

In the nervous system the motor cells of the anterior cornu of the cord are reduced in number and there is also a diminution in the number of fibers in the anterior nerve-roots, which are small and deficient in myelination. Fibrosis of the thyroid and thymus has been reported (Spiller).

Oppenheim believed that the malady was the result of delayed development of the muscles and possibly also of the anterior horn cells. Holmes and Collier hold that the changes are regressive lesions, while Cattaneo suggests perverted internal secretion.

ETIOLOGY.—This has not been determined. The disease appears during the first few years of life, being congenital in the majority of cases, though not familial. The two sexes are affected about equally. Cases have been reported in association with myopathy (Sylvestri), and the disease has in a few instances followed an acute infection, such as bronchitis. Signs of physical or mental arrest at birth have been absent.

PROGNOSIS.—The disease tends toward gradual improvement without complete recovery. Progress is most marked in the muscles least affected.

Implication of the respiratory muscles may lead to a fatal termination.

TREATMENT.—Tonics, such as iron, quinine, and strychnine, are recommended. The nutrition of the affected muscles should be stimulated by massage and passive movements.

Braces or mechanical appliances of any sort are contraindicated, and the child should be encouraged to help himself as much as possible.

In a case attended with acholia, bile salts or dried oxgall caused an increase

in muscular strength. Powis and Raper (*Quart. Jour. Med.*, Jan., 1917).

Case in an infant in which the symptoms strongly suggested amyotonia congenita but creatin and creatinin excretion were much below normal. Upon addition of creatin in **beef broth** to the mother's milk, muscular development took place, ceasing whenever the beef broth was stopped. **Massage** and **codliver oil** were also ordered. Brereton and Cameron (*Can. Med. Assoc. Jour.*, Nov., 1923).

With reference to muscular adynamia in general, in the absence of paralysis, the writer urges the use of **caffeine**. Benefit may also result from **dextrose infusions**. Additional use of **insulin** will probably do good. I. Pal (*Wien. klin. Woch.*, May 29, 1924).

MYOPATHY, OR MUSCULAR DYSTROPHY.

SYNONYMS.—Idiopathic muscular atrophy; primary myopathy; progressive muscular dystrophy.

DEFINITION.—Under the general heading myopathy are included a number of forms or types of muscle disorder, frequently hereditary or familial, having in common an onset at an early age, atrophy, and the absence of fibrillary tremors and reactions of degeneration. The atrophy may be associated with true hypertrophy or pseudohypertrophy.

The appearance of two or more of the different types of myopathy in the same family, and the occurrence of transition forms of the disease, establish the unity of the group.

HISTORY.—To Meryon, from a published report of a case with necropsy in 1852, belongs the credit of ascribing pseudohypertrophic paralysis to a primary disease of the muscles, although the first authentic clinical description was made by Bell in 1830. Duchenne, in 1868, was the first to use the term "pseudohypertrophic paralysis." The juvenile form was so designated by Erb in 1882, and the facioscapulohumeral

type was described in 1884 by Landouzy and Dejerine.

SYMPTOMS.—The onset of the disease is gradual, an awkwardness in walking being usually the first symptom noted. The child falls readily and rises with difficulty. Ascending the stairs becomes difficult or impossible. Later a change in the size of the muscles is noted, consisting of either an increase or a diminution. In either case the alteration in size of a muscle is associated with a diminution of its power, and muscles primarily enlarged may later show atrophy. The extremities, especially the proximal portion, and the trunk are commonly affected, and, while the malady is bilateral, it is not always symmetrical. In the upper extremity the muscles of the shoulder-girdle, including the deltoid, trapezius, pectoralis major (sternocostal portion), latissimus dorsi, serratus magnus, rhomboids, and infraspinatus, are involved. Next in frequency follow the anterior arm muscles, the biceps, and the brachialis anticus. The supinator longus is also frequently affected. In the trunk the erectores spinæ are often involved, the abdominal muscles less frequently. The pelvic muscles are apt to be wasted, and in the lower extremity the flexors of the hip, quadriceps and thigh adductors, calf muscles, and the peroneal group usually suffer.

The shoulder-blades are apt to become abnormally mobile ("loose shoulders"), riding upward and flaring out. As pointed out by Brissaud, there is an apparent lengthening of the neck from this drooping.

Curvature of the spine is at times a conspicuous symptom. Lordosis may occur as the result of weakness

of the muscles, which produce extension at the hip, causing a tilting forward of the pelvis and a compensatory throwing backward of the upper part of the trunk to keep the center of gravity over the feet. The lordosis disappears when the patient is seated, the pelvis then resting on the tubera ischii. Lordosis may also occur as the result of wasting of the abdominal muscles, and scoliosis may develop from unequal weakness of the spinal muscles.

The child walks with a curious waddling gait, owing to the weakness of the extensors of the hip, and has great difficulty in ascending steps, because of the weakness of the extensors of hip and knees. When seated he rises by helping himself with his arms, placing his hands on his knees or thighs. If placed on his back on the floor he first rolls over on to his abdomen, then brings himself to a kneeling position by the aid of his arms, and next into a stooping position with his hands on the floor. He then straightens his legs and brings them toward the vertical by pushing backward with his hands, gradually bringing them closer to his feet. When this is accomplished he places one hand on the corresponding knee and with the other hand still on the floor pushes with both until he gains sufficient extension of the hips to enable him to place both hands on his knees, after which it is a simple matter to bring the trunk upright. This process of "climbing himself" is very characteristic of the condition.

The face is sometimes affected, causing the patient to have a rather vacuous or somnolent expression. Weakness of the orbicularis palpebrarum may cause difficulty in clos-

ing the eyes, and wasting of the orbicularis oris causes drooping of the lower lip and apparent pouting—the so-called "tapir snoot."

Deformities from permanent changes of joint position constitute a late and distressing group of symptoms. Contractures result from the action of normal muscles unopposed by the wasted antagonists.

Electrical reactions show only a quantitative reduction in excitability of the wasted muscles to both faradic and galvanic currents. Reactions of degeneration do not occur in myopathy.

The knee-jerk is normal, diminished, or absent, according to the degree of involvement of the knee extensor muscles.

Sensation is normal and the sphincters never involved. Fibrillation is only rarely observed. Arrested mental and physical development are occasionally found in association with myopathy. Congenital bony anomalies and osseous atrophy have been observed in rare instances.

Various forms of myopathy are recognized. The *juvenile type*, or brachial form of Erb, attacks chiefly the muscles of the shoulder and upper arm and appears most commonly in the older patients.

The *infantile form*, or facioscapulo-humeral type of Landouzy-Dejerine, affects primarily the muscles of the face, shoulder-girdle, and arm.

The *pseudohypertrophic form* is characterized by a false hypertrophy of some muscles, combined with atrophy in others.

Primary atrophy is usually limited to the muscles of the upper half of the body. It is, however, extremely rare for any of the muscles of the

face to be involved, and the same is true of the neck muscles. Gowers states that he has seen wasting of the clavicular portion of the sternomastoid.

In the upper extremity, in addition to the infraspinatus, the supraspinatus may be hypertrophied, and not infrequently the deltoid. The pectoralis major is never enlarged, but it is common to find it atrophied in its lower half. The latissimus dorsi and teres major may also show wasting. The biceps and triceps are sometimes enlarged, but more frequently atrophied. Muscles of the forearm rarely show any change, and the intrinsic muscles of the hand are almost never involved, the condition presenting in this respect a marked contrast to progressive muscular atrophy of spinal origin.

Of the truncal muscles the lumbar group generally present some enlargement. In the lower extremity, flexion of the hip is usually so distinctly affected as to indicate weakness of the flexor muscles of this joint. The muscles of the calf (gastrocnemius and soleus) are most frequent among those showing hypertrophy. The anterior tibial muscles are sometimes enlarged.

Case of progressive muscular dystrophy of interest because of the onset at the age of 16, the absence of heredity, and the presence of some of the symptoms of all three subgroups. Definite muscular weakness first appeared in the right upper extremity, next the left, then the back, hips and lower extremities. Shortly after the muscular weakness set in, atrophy of the shoulder-girdle muscles was noted, progressing until typical winged scapulæ resulted. There was slight weakness of the orbicularis oris; weakness of the anterior and posterior trunk groups;

weakness of the posterior thigh and anterior leg groups; no atrophies below the waistline, but possibly some pseudohypertrophy of the thigh and calf groups. The mode of arising from a supine to an erect position was characteristic. The electrical reactions showed only a quantitative change in excitability. Finlayson (*Neurol. Bull.*, Nov.-Dec., 1919).

DIAGNOSIS.—In a typical case the age of the patient, the peculiar waddling gait, the difficulty in ascending stairs, and characteristic manner in rising from the floor, in association with wasting of the muscles unaccompanied by fibrillation or reactions of degeneration, should afford an easily recognizable picture.

Congenital spastic paraplegia bears a superficial resemblance to pseudohypertrophic paralysis in the gait, the weakness of the legs, and the enlargement and contraction of the calf muscles. In the former affection, however, the reflexes are increased, Babinski's sign is present, and the legs are markedly spastic.

Infantile palsy has an abrupt onset, is not progressive, and has the electrical reactions of degeneration. It is from the simple atrophic form of myopathy, rather than the pseudohypertrophic form, that a diagnosis would have to be made, as there would be no muscle enlargement in poliomyelitis.

Muscular atrophy following polymyositis presents no pseudohypertrophy, although the electrical irritability of the muscles would show the same quantitative diminution. In polymyositis there would also be a history of pain in the early stage.

PATHOLOGY.—The diseased muscles are pale yellow in color and, as Gowers long ago pointed out, re-

semble masses of adipose tissue. Under the microscope are seen both atrophied and hypertrophied muscle fibers, with a marked infiltration of fat tissue between the fiber bundles.

Indeed, in some instances the relation is reversed, the bulk of the mass being adipose tissue with small bands of muscle fibers seen scattered here and there through the fat. The fibers may show vacuolation, granular degeneration, occasionally waxy degeneration, and the cross-striations may be faint. There is an increase of the muscle nuclei and the fibrous interstitial tissue is often greatly augmented. Such changes as have been found in the nervous system have been inconstant and probably accidental, the anterior horn cells of the cord and the motor nerves being invariably normal.

Apparently the muscles waste because of a congenital anomaly of development. In this connection Gowers called attention to a form of congenital tumor—myolipoma—a section of which is almost identical with a section from a diseased muscle in pseudohypertrophic paralysis.

Of 7 living members of a family showing a somewhat atypical form of progressive muscular dystrophy resembling Erb's infantile type, benign and slow in progress, 4 showed distinct X-ray changes in the pineal gland. A fifth showed an enlarged sella turcica. Pineal disturbances probably play an important rôle in the pathogenesis of progressive muscular dystrophy. Timme (Arch. of Int. Med., Jan., 1917).

ETIOLOGY.—The onset of the disease is usually during early childhood, less frequently at about the time of puberty. It may not appear before young adult life, and is seen

rarely in middle age. The malady is both hereditary and familial, but sporadic cases are by no means infrequent. It attacks the males chiefly, but is transmitted by the females whether they themselves have been affected or not.

Of 12 children in a family reported, 7 had progressive muscular dystrophy. There was no evidence of direct inheritance. The symptoms appeared insidiously at about the age of 7 years in each case. The basal metabolism ranged from -22 to $+10$. H. P. Mills, T. H. Haines and M. A. Sessions (Arch. of Neurol. and Psych., Jan., 1924).

The generally accepted view of the muscular dystrophies as primary diseases of muscle is a negative conception, being essentially based on the negative findings in the nervous system. Phenomena sometimes observed in these cases, *viz.*, marbled appearance of the skin, contractures, trophic bone changes, changes in the heart muscle, intellectual impairment and endocrin disturbance, suggest that the muscular atrophy is merely the most prominent manifestation of a more generalized pathological process. As there is much evidence of a dual—somatic and sympathetic—inervation of the skeletal muscles, disease of the sympathetic supply is suggested as a possible determining cause of these dystrophies. The gradual loss of power and wasting might be a consequence of secondary involvement of the somatic nerve fibrils by the changes in the muscles and interstitial tissue which result from disease of the sympathetic nerve-supply. Disturbances of pituitary function are met with in muscular dystrophy with a frequency which can hardly be accounted for by coincidence. Among the cases cited is one of pseudohypertrophic paralysis with adiposity and defective sexual development. The writer knows of a number of similar cases. Other patients present appearances suggestive of acromegaly. Hypoglycemia has been noted

by several observers. Edwin Bramwell (Lancet, Nov. 28, 1925).

COMPLICATIONS.—As already mentioned, imbecility is sometimes associated with myopathy, which is not surprising when one considers that both are the result of congenital anomalies of development. Oppenheim observed a case of myopathy in combination with Little's disease.

PROGNOSIS.—The disease, as a rule, is steadily progressive, but in rare instances may remain stationary. When it appears early, duration of life is apt to be short, the child rarely reaching adult years. When it is late in developing, the possibility of an arrest of its development is greater. In any event, however, the prognosis is grave, the patient dying usually from some intercurrent affection, or from implication of the respiratory muscles and diaphragm.

While, usually, the earlier the condition starts the more rapidly it is progressive, this is not always so. One of the writer's untreated cases 9 years old, ill 6 years, is practically bedridden. Another case, 12 years old, ill since 3 years of age, and another 15 years old, ill since 2 years, have shown a slower progress of the paralysis. Six sisters all developed the condition at about 50 years of age. The usual tendency of the disease is to progress to complete invalidism, with exacerbations lasting one to several weeks. These increase in severity, duration and frequency, and death often comes at 16 to 18 years in the earlier cases, while the slower cases continue on to old age. Clifford Wright (Cal. and West. Med., Aug., 1925).

TREATMENT.—Care should be taken to avoid overexertion or strain upon the already weakened muscular apparatus. Tonics improving the general physical condition may cause a temporary retardation of the malady.

Carefully regulated volitional exercises, massage, and passive movements are of some value.

Case of general progressive muscular atrophy of 4 years' standing in which blood examination showed almost total absence of sugar and creatinin. The legs, arms, and shoulders were much atrophied and the diaphragm ptotic, with loosely attached viscera. The patient was put to bed, without pillows, to raise the diaphragm to about the normal position. For several periods of $\frac{1}{2}$ hour each he was placed in the hyperextended position, with a pillow under the dorsal spine and the hands clasped under his head. Light massage and stimulating baths were given, together with small doses of adrenalin and pituitary. Improvement was definite after 3 weeks. He was fitted with a brace to hold the body fully erect, allowed up for short periods, and given exercises for the chest and trunk muscles. A generous diet was given. Returning home after 9 weeks he kept up the exercises and wore the brace for 3 years. He was then fully recovered, and remained well thereafter. Goldthwait (Boston Med. and Surg. Jour., Apr. 27, 1922).

Electricity, if used at all, should be applied with great care, as it is capable of doing quite as much harm by overstimulation as it is liable to do good.

Orthopedic operations, such as tenotomy for a shortened tendo Achillis, and tendon transplantation, are advocated by Oppenheim, Hoffa, Kuh, and others, but can obviously be only of transient value.

Fixation of the shoulder-blade to the trunk or of the two blades to each other has been done with some success (Eiselsberg, Raymond). The writer, in a case of subscapular myopathy, found a mechanical device of service and of comfort to the patient by keeping the scapula in place.

Scapulopexy was successfully performed by Pauchet in a case of juvenile muscular dystrophy (Erb's type) in which the shoulder muscles of both sides were markedly involved. The insertions of the 1st to the 9th ribs were exposed by a longitudinal incision 2 fingerbreadths from the spinous processes and parallel with these; the inner margin of the scapula was freshened, and likewise the corresponding points of the ribs. A number of holes were bored through the scapula, and wires pulled through, twisted around the rib, and fastened in place. The outcome, after bony union, was excellent; the scapula occupied its normal level, and the arm could be raised to the horizontal plane.

Following pituitary symptoms in cases of progressive muscular dystrophy with pseudohypertrophy emphasized: Large, round head; round face; spaced teeth; heavy central incisors; pituitary type of hand; smooth, mottled skin; poor nails, and sexual underdevelopment (all found in anterior lobe insufficiency and girdle obesity); high sugar tolerance and weak pulse (found in posterior lobe conditions). In most cases, the X-ray shows an undersized sella turcica and rarefaction of the bony tissues, both indicative of pituitary disturbances. That the muscular dystrophies are endocrinopathies seems borne out by the frequent association with Graves's disease, Addison's disease, acromegaly or myxedema, and in that many cases show pigmentation, vitiligo, hypoglycemia, asthenia, and other endocrin symptoms. Several cases have shown spontaneous cure at puberty. In the treatment, aside from orthopedic supervision, including **bracing** for support, correction of deformities, and graduated **muscle training**, the writer, dealing with 19 cases, has for several years used pituitary products—**whole pituitary** by mouth, **antuitrin**, and when indicated, **pituitrin** hypodermically; also occasionally **adrenalin** and small doses of **thyroid**. Many patients were benefited to the extent that the paralysis seemed non-progressive and the exacerbations less frequent and less

severe, and in 2 or 3 patients there was very marked improvement. The mental condition of all cases was greatly improved. C. Wright (Cal. and West. Med., Aug., 1925).

FAMILY PERIODIC PARALYSIS.

DEFINITION.—A disease characterized by periodically recurring, more or less general, flaccid muscular paralysis, usually hereditary, with intermissions between attacks.

HISTORY.—Family periodic paralysis, which is comparatively rare, was described by Cavaré in 1853, and in somewhat greater detail by Romberg in 1857. Edward W. Taylor, in 1898, found 53 cases in the literature, and in 1902 64 cases were collected by Oddo and Audibert.

SYMPTOMS.—The essential clinical feature of the disease is a series of attacks of muscular paralysis, developing usually at night, the patient waking up to find loss of power affecting part or all of the extremities, neck, and trunk. If an attack develops when the patient is awake it is of gradual onset, reaching its height within a few hours. The attack is sometimes preceded by such prodromal symptoms as malaise, headache, backache, bulimia (Holtzapple), increased frequency of urination, and paresthesias. The lower extremities are most constantly affected and may be alone involved, but the malady frequently attacks all the voluntary muscle system except that part supplied by the cranial nerves. In an isolated instance the face was affected. Duration of the attack is from a few hours to a day, two days, or rarely a week, the paralysis passing off gradually. Recurrence takes place at irregular intervals, varying from a few days to weeks or even years. During the attack conscious-

ness is preserved, the sphincters are unaffected, and sensation is normal.

During the paralytic phenomena the electrical reactions are found to be diminished or abolished; reactions of degeneration are not present. The tendon reflexes are also diminished or lost, returning to normal in the interval between the attacks. Evidence of cardiac dilatation and irregularities in cardiac rate and rhythm have been observed.

An interesting observation is that of Holtzapple, who found migraine alternating with the paralytic attacks. Indeed, the history of an individual attack has many features in common with migraine, such as the paresthetic aura or prodromata, perverted appetite, and the gradual onset, duration, subsidence, and recurrence.

PATHOLOGY.—The muscles have been studied both after necropsy and from pieces excised during life. The necropsies were obtained in 2 cases from Holtzapple's series and revealed nothing from which the symptoms could have resulted. Crafts, Singer, Goldflam, and Oppenheim have examined excised portions of muscle, and report such changes as waxy degeneration, vacuolation, and fibrillary hypertrophy. No changes have been found in the nervous system.

Chemical studies are of interest. The toxicity of the urine has been found to be somewhat increased during an attack of the paralysis (Goldflam, Goodbody), and a general reduction in the excretion of urea has been noted (Holtzapple), although increased in one instance during the attack. In another isolated instance acetone was frequently found in the urine during the attack. Of more importance, however, is the observa-

tion by Mitchell, Flexner, and Edsall of a diminished excretion of urea for some time before the attack and a marked increase subsequent to it. The very inconstancy of the toxins found shows the present obscurity of the etiology.

An analogy between the attacks of family periodic paralysis and those of myasthenia gravis has been referred to and a study of the thymus in its relation to the former condition suggested (McCarthy).

That the palsy has its origin in the muscles themselves, and not in the peripheral or central nervous system, is shown by a loss of the muscle irritability to mechanical and electrical stimuli during the paralytic attacks.

ETIOLOGY.—The marked hereditary character of this disease at once attracts our attention in considering the etiology. While isolated cases have been reported, the disease has generally been found occurring in families, extending through several generations and transmitted through either sex. Holtzapple found 17 cases appearing in 4 generations, and Taylor 11 cases in 5 generations.

A study of the heredity aside from the transmission of the peculiar paralysis has revealed nothing of importance except in association with migraine to an extraordinary degree in one family (Holtzapple).

The paralysis commonly appears about the age of puberty, but may occur as early as the second or third year, or as late as 30 or 35.

Exposure to cold (Rich) and overexertion have been mentioned as exciting causes; likewise emotion, shock, overeating, and menstruation. Infections have not appeared to play

any rôle in the etiology, either as underlying or exciting factors.

TREATMENT.—Some of the earlier cases of family periodic paralysis seem to have yielded to **quinine**, and large doses of **potassium citrate** are asserted to have been helpful, yet in the majority of instances no measure at our disposal seems to be of service.

GEORGE E. PRICE,
Philadelphia.

MUSCLES, SURGICAL DISEASES OF.

CONTUSION.

A simple or uncomplicated injury to muscle alone is not a common condition. More frequently the muscle injury is associated with pathologic change of overlying tissue or of the deeper osseous framework.

SYMPTOMS.—The physical signs of muscle contusion vary with the character and severity of the injury and the muscles involved, and according to whether the injury took place during relaxation or contraction of muscle fiber. In contusion of muscles the result of blunt force, there may be a temporary ischemia of the part, with rupture of but few blood-vessels and little external evidence of injury. In the contusions associated with the ordinary fractures, on the other hand, there occurs a local bluish-green discoloration, which appears early or late according to the state of integrity of the deep fascia, the extent of involvement of blood-vessels, etc. With this are associated pain, tenderness, swelling, and limitation of movement. Anesthesia or paresthesia may be present because of pressure on main trunks or branches of the peripheral nerves.

PATHOLOGY.—Muscular contusion is attended with rupture of capillaries, small veins or the smaller arteries, with resulting escape of blood between the muscle cells and rupture of the sarcolemma or the muscle fibers. If the lesion is not extensive and proper methods to encourage repair are instituted, complete regeneration of the injured fibers may be expected, with return of function; if, on the other hand, the lesion is extensive and proper treatment has not been instituted, the injured fibers will be replaced by fibro-connective tissue and loss of function take place.

TREATMENT.—Absolute rest of the involved muscles should be instituted. If the case is seen early, previous to marked swelling, a thin layer of **absorbent cotton** over which is applied a snug **bandage** forms the best temporary dressing. If swelling is pronounced, a **moist compress** of saturated solution of **magnesium sulphate** may be applied.

Several days after the injury, a fluctuating swelling may appear. In this event, the accumulated serosanguineous fluid should be withdrawn by **paracentesis**, a 16 gauge needle being used. A firm **bandage** should then be applied.

In children and very nervous patients **splinting** may be necessary.

LACERATION.

Muscle tissue is not very resistant to direct application of forces tending to lacerate it, and is thus relatively easily torn or reduced to a pulp inside of its sheath. Gunshot and stab wounds are among the conditions involving this type of muscle injury.

Where the extent of muscle tissue destruction is small, very complete

healing may subsequently occur, the muscle so regenerating as to preclude microscopic detection of the site of injury. Where, on the other hand, extensive crushing, especially with retraction of the ends of the muscle, has occurred, healing is far less perfect, taking place mainly through the deposition of dense connective tissue between the severed ends.

TREATMENT.—If the case is seen within eight hours after the injury, a **débridement** and complete **closure** should be done. Proper management of this type of case is important and can be divided into three distinct stages: *First Stage.*—**Preparation of the wound.** A sterile piece of gauze is placed over the wound, and the surrounding skin for a distance of 2 inches (5 centimeters) or more, if possible, is shaven, washed with **ether** and **alcohol** and painted with **tincture of iodine**. The wound is then irrigated with **normal saline solution** and its depths painted with **tincture of iodine**. Next, the skin is again painted with iodine. Finally, the skin and the wound are isolated by application of sterile dressings.

Second Stage.—**Débridement.** Any devitalized or questionable dead tissue or any foreign material is next removed, the instruments used are discarded, the wound and skin is again painted with tincture of iodine, and the operative field redraped.

Third Stage.—**Closure.** Using fresh instruments, the muscles and deep fascia are closed with No. 0 chromic catgut and the skin and subcutaneous tissue with interrupted silkworm gut sutures. Finally, a large **moist dressing** of **alcohol**, 40 per cent., saturated solution of **boric acid**, 30 per cent., and **glycerin**, 30 per cent., is applied.

If the operation is delayed and twelve hours have elapsed, the technique should be modified in that sections of **Penrose drain** are to be placed between alternate silkworm gut sutures; or, if there is considerable oozing from muscles, these drain sections can be placed between the interrupted sutures in the deep fascia. A moist dressing is then applied. The Penrose drains are removed at the end of twenty-four hours. If more than twelve hours have elapsed, it is probably best to institute **Carrel-Dakin treatment** until the wound is sterile; a secondary closure is then done.

RUPTURE.

A muscle may become partially or completely ruptured by reason of its sudden and severe contraction. Atrophy and degeneration are common predisposing causes. A slight degree of rupture involving only a few muscle fibers is common. This happens in *lawn-tennis leg*, where fibers of the gastrocnemius or plantaris are ruptured. The usual history is that after a sudden twisting motion the patient experienced a pain in the calf; the muscle becomes rigid, and on examination a small depression may be palpated. The rupture may be attended by an audible snap. There is great pain on attempted movement. Tenderness is noted, and swelling is soon added; ecchymosis may appear.

In *riders' thigh*, the fibers of the adductors of the thigh are torn to a greater or less degree. There is marked pain, tenderness, swelling and ecchymosis. A groove may be felt in the muscle.

Muscular rupture in the abdominal wall involves usually the rectus, rarely the obliques. Such rupture has occurred during

labor, and may take place even in normal subjects. In persons whose muscles have been weakened by typhoid fever or other debilitating disorders, slight exertion, such as coughing or rising to the sitting posture, may suffice to rupture an abdominal muscle. In these cases healing usually occurs without intervention for suture.

Other muscles occasionally ruptured include the quadriceps extensor, biceps humeri, triceps, and deltoid.

TREATMENT.—In a muscle rupture of the type of lawn-tennis leg the treatment consists of **strapping** the part with adhesive plaster. Immediate **exercise** should be instituted, the patient placing the heel on the ground despite accompanying pain. The adhesive straps should be replaced when they become loose. With this form of treatment the results are apparently better than if absolute rest is instituted. Even after three weeks' limitation of movement, however, recurrences are rather frequent following active exercise.

In general, in partial muscular rupture, **strapping** may be sufficient treatment. In complete rupture, however, **myorrhaphy** must be performed. An incision corresponding to the long axis of the muscle is made; blood clot is removed, the bleeding controlled, and the muscles relieved of all tension. Approximation is obtained by using interrupted mattress sutures of chromic catgut No. 0 or 1. The fascia and skin are closed in the usual manner. The muscles are to be kept in a state of relaxation for three weeks.

In rupture of the biceps, flexion of the forearm in pronation when the biceps is tense is more forcible than when the forearm is supinated and the biceps relaxed (*Hüter's sign*). Tears of the muscle usually lead to hematoma, more noticeable during contraction, whereas in rupture of the tendon, this is absent or slight. If rupture is

complete or nearly so, prompt **operation** is indicated. If the long head is ruptured at its attachment to the lip of the glenoid or near its upper end, the writer slips the tendon of the long head through a portion of the short head near its coracoid attachment, then fastens it to the coracoid process and fortifies the fixation by 2 sutures in the tendon of the short head, where it emerges. For tears, **active exercise** is the best massage. **Rest** and movement are both important healing factors. Convalescence is shortened by **radiant light and heat**, and **manual massage**. **Passive movement** should be carried out after the 3d week, and **active** after the 4th. E. L. Gilcreest (Jour. Amer. Med. Assoc., June 13, 1925).

HERNIA OF MUSCLE.

Hernia of muscle consists of the obtrusion of muscle tissue through its sheath. It is usually the result of injury. The tumor is prominent when the muscle is at rest, disappears when the muscle is passively extended, diminishes in size on active motion, and disappears when the muscle is contracted against opposition.

TREATMENT.—The hernia should be exposed, the protruding portion if necessary **excised**, the wound in the muscle closed. The **fascia** is then **undermined** for a short distance around the hernial opening to relieve tension, the **hernial opening closed** with interrupted sutures, the **fascia being imbricated** if possible, and the skin wound closed.

STRAIN.

This term is generally applied to a condition of longitudinal stretching of a muscle or its tendinous extremity, with rupture of a few of the fibers. The affected muscle becomes tender, swollen and rigid, and gives pain on active motion. Strain of the long head of the biceps in base-ball players is sometimes termed "glass arm." Strain of the pronator teres in tennis players has been called "lawn-tennis arm." Strain of the

psoas, if on the right side, may to some extent simulate appendicitis. In strain of the back, muscle strain is frequently combined with strain of vertebral ligaments. Among other muscles commonly the seat of strain are the deltoid, pectoralis major, hamstring muscles, and the muscles of the calf.

TREATMENT.—The region involved should be placed at rest in a position such that the affected muscle is relaxed. Splints may be used or, in some instances, as in the case of the calf muscles or back, strapping with adhesive plaster resorted to. Hot applications may be employed to alleviate pain. Massage should be started promptly upon subsidence of the acute symptoms.

OSSIFICATION.

This condition follows repeated trauma, as a result of which, not uncommonly, bone formation will take place in the body of a muscle. Repeated localized strains may induce local inflammation, with consequent partial ossification of the muscle concerned. Ordinary examples of this are the "rider's bone" sometimes met with in the origin of the adductor of the thigh, and the so-called "drill bones" in the insertion of the deltoid. The rider's bone occurs in persons who do rough horseback riding. Ossification in a deep-lying muscle is not recognized during life, but in superficial muscles it can generally be detected by pressure. Syphilis has likewise been considered a cause of ossification. (See also MYOSITIS OSSIFICANS under MUSCLES, DISEASES OF).

TREATMENT.—Where the intramuscular bone formation results in pain and impairment of function of the affected muscle, the treatment consists of excision, all milder procedures having been found ineffective.

DISLOCATION OF MUSCLES.

The long tendon of the biceps may be displaced from its groove. Occa-

sionally the tendons of the peronei are dislocated over the external malleolus in severe wrenches or sprains. Dislocation of the tendons of the extensors of the wrist may similarly occur. Such displacements are facilitated by coincident laceration of synovial sheaths and fasciæ, and may accompany a fracture. They are not exclusively dependent upon violence, however, for their production. Thus, dislocation of the long head of the biceps may occur in rheumatoid arthritis of the shoulder-joint.

Pain and loss of function of the involved muscle are the customary symptoms of dislocation. It may be possible to feel a displaced tendon and note a hollow in its normal situation.

TREATMENT.—This consists of relaxation of the involved muscle and manipulation. Strapping with adhesive plaster should be carried out, or a snug bandage applied. This support should be continued for at least three weeks. If such treatment fails, operative intervention for suture of the torn sheath may be required.

ATROPHY.

In simple atrophy the muscles decrease in size and become flabby. This condition is most frequently seen when muscles are rendered inactive by splinting for fracture. Under these circumstances the muscle fibers become thin, and if to inactivity there is added pressure, the atrophy is increased and contraction from resulting degeneration commonly occurs.

Pronounced muscular atrophy is frequently observed following injuries to the peripheral nerves, especially if the parts have not been properly splinted, permitting an over-stretch-

ing of the muscle fibers, and if proper physiotherapeutic measures—massage, electricity, etc.—have not been instituted.

The writer has observed marked atrophy of the deltoid without visible contraction and beginning reaction of degeneration, due to gunshot wound involving the circumflex nerve, show contraction and diminished atrophy within a few weeks following the application of an aeroplane splint. Atrophy of the interossei and lumbricals together with contraction of the flexor tendon are responsible for the *claw hand* following complete interruption of continuity of the median and ulnar nerves. Anterior poliomyelitis is responsible for atrophy of the muscles *en masse*.

PROPHYLAXIS.—Splints should not be too tightly applied, and the patient should be instructed to notify the attending physician if swelling or pain develops in the affected parts. The physician should see the limb daily for the first three days. Gentle massage should be instituted early.

TREATMENT.—This consists of removal of the cause and the application of physiotherapeutic measures. Wounds of nerves should receive early surgical treatment, and proper support of affected muscles should be provided.

When a limb has merely become thin through disuse while in a splint, and if normal resolution does not soon follow its release, light massage will, according to Davis, bring about rapid improvement. **Effleurage**, with the strokes directed toward the trunk (to activate the circulation) and made with the palm of the hand or its radial border, is indicated at first. Later, when the limb has become stronger, **pétrissage**, i.e., seizing the tissues with both hands and raising them (as a cat is lifted by the neck) repeatedly, followed by kneading of the parts thus raised—should be resorted to.

Strychnine may also be administered internally.

ISCHEMIC MUSCULAR ATROPHY.

Ischemic atrophy, or *Volkmann's contracture*, is caused by interference with the circulation of the part, although pressure on the nerves may exert some influence in the condition. The circulation is interfered with by unduly tight applications of splints and dressings, or by too prolonged use of the elastic constrictor. Cases are on record, however, in which pressure of splints could not have been responsible; in these cases, the escape of blood into the muscle may have been the cause.

The forearm is the region most commonly involved. Pain may or may not be present. The hand becomes swollen within a few hours; the phalanges become flexed, and paralysis of the muscles follows. The muscles are hard, swollen and tender. When recovery takes place, a permanent contracture is left. When the muscles of the forearm are affected, the phalanges are flexed on each other, but the metacarpophalangeal articulation remains extended. The phalanges can be extended only when the wrist is flexed. If muscle destruction has been more extensive, the wrist becomes flexed as well as the fingers.

TREATMENT.—The prognosis in this condition has been greatly improved by the use of the **Jones method** of gradual correction. With the wrist forcibly flexed in order to relax the thumb and fingers, straight splints of metal are applied separately to each of these members, which are thus gradually straightened. The patient is next encouraged, with the fingers

held straight and wrist released, to extend the metacarpophalangeal joints. Such extension having been attained, in the course of some days, the entire hand to the wrist is splinted and the flexion at the wrist gradually corrected. Finally, full extension is maintained for some weeks until all tendency to recurrence of the deformity has disappeared. From this point on the circulation in the tissues generally improves and the member resumes its normal appearance unless nerve destruction has coexisted. **Rugh** has devised a special splint which facilitates the straightening process.

If the conservative treatment, continued for three months or more, fails, an **operation** consisting of incision over the contracted tissues in the forearm, freeing of adherent fascia, liberation of nerves, and lengthening of the contracted tendons is in order.

Case of **Volkman's** contracture limited to the pronator quadratus in a boy of 6 years, following marked pressure for retention of a fracture of both bones of the forearm. When he was seen $2\frac{1}{2}$ years later the forearm was held rigidly in extreme pronation on account of contraction of this muscle. Through an incision at the anterior edge of the ulna just above the wrist, the pronator quadratus was exposed by lifting the ulnar nerve and flexor tendons forward and the tight fibrous muscle cut across near its origin. The forearm could then be supinated and was **splinted** in this position. Later a splint was worn at night for several months. **Active exercises** compelling supination were carried out. There was final restoration of supination to about $\frac{2}{3}$ the normal extreme. **J. S. Stone** (Boston Med. and Surg. Jour., Dec. 17, 1925).

CONTRACTURE.

• Permanent fixation of a muscle in the contracted state may, as described by **Davis**, be caused by a large number of factors: Inflammation of local or remote tissues;

traumatic or toxic agencies, etc. Hemiplegia is often complicated with contracture of all the muscles of the upper extremity. The arm is usually held against the body, the hand being flexed upon the forearm and the latter upon the arm: a general contracture of the flexors. In some cases, however, the forearm is merely flexed upon the arm, the latter being free at the shoulder. When this variety occurs in a young woman, hysteria is to be suspected. Contracture of this character may also be due to rheumatism or syphilis, the biceps, *e.g.*, being sometimes the seat of an exacerbation of either disease.

Permanent contracture often follows severe traumatism when appropriate curative measures are not immediately instituted. Severe burns are apt to be followed by cicatricial contracture when the region of the elbow or the palmar tissues are involved. Chronic inflammation of a muscle, descending neuritis, persistent irritation along some portion of the motor tract, or prolonged disuse of a muscle if it remains in a given position, weakened action of an antagonistic muscle whether of central or peripheral origin, contiguous bone or joint disease, and tumors pressing upon a given set of muscles or its nervous supply are all capable of giving rise to contracture.

The lower extremities are susceptible to the same influences as the upper. Aside from the neurologic disorders, spasmodic rigidity, and other conditions which sometimes require tenotomy or myotomy, contraction of the thigh muscles due to dislocation or hip disease is occasionally witnessed.

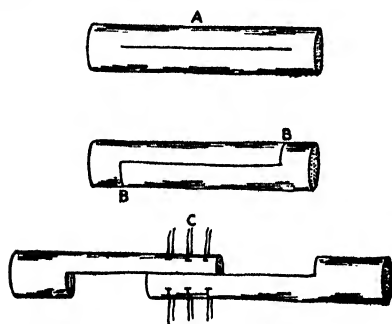
Non-traumatic contractures are usually the result of cerebral or spinal lesions, and, in children, of infantile paralysis. Spinal inflammatory disorders are usually attended by marked flexion at the hip and knee.

True contracture is differentiated from temporary rigidity, such as is witnessed in the early stage of inflammation of a joint and in hysteria, by the fact that in these disorders the muscles relax under an anesthetic, whereas in permanent contracture they do not.

TREATMENT.—The causes of contracture being many, the treatment varies in accordance with the needs in the individual case. Thus, in rheumatic and in syphilitic contraction of the biceps, a course

of **potassium iodide** is of importance to antagonize the cause and prevent recurrence after **tenotomy**—the second phase of the curative measures indicated. The biceps tendon is easily cut by passing a tenotome flatwise beneath it from within outward (thus avoiding the artery) and cutting upward with a gentle sawing motion. The wound having been closed, the arm is fastened to a **straight splint**, in **extension**, and **passive motion** later instituted.

Lengthening of tendons to overcome contracture has been performed by Keen, Anderson, and others in the manner indicated in the annexed cut. Properly performed, this operation gives excellent results.



Anderson's operation for lengthening a tendon.

Another operation that has been employed is section of the muscle itself—**myotomy**. Macewen advocated the making of several **V-shaped incisions into the muscle**.

Additional measures which may be of service are **massage**, **friction**, **electricity**, and **passive movements**.

In contractures of the knee due to inflammatory processes affecting the joint, where forcible mobilization has failed, the writer makes **injections of 60 per cent. alcohol** into the nerve branches to the contracted muscles, especially to the semimembranosus, semitendinosus, and long head of the biceps. The joint is then **immobilized** for a time in slight hyperextension. After a period of rest in bed, all evidence of flexor contracture disappears. Maragliano (*Chir. d. org. di movimento*, Dec., 1921).

Case of reflex contractures of the muscles of the left upper limb following a fracture of the neck of the

scapula. Recovery took place upon carrying out **periarterial sympathectomy** on the subclavian artery. Brezovnik (*Casop. lek. cesk.*, Feb. 28, 1925).

TORTICOLLIS (WRY NECK).

This condition is characterized by an altered position of the head due to contraction of the muscles on one side of the neck. The head is drawn down on the affected side and rotated to the opposite side.

Wry neck frequently begins in childhood and is sometimes congenital. In acquired torticollis, cold or rheumatism have been noted as causes; likewise, throat affections, glandular inflammation, vertebral disease, and contraction from burns. In most instances acquired torticollis is due to disease or injury of some structure of the neck, with resulting nerve irritation and active contraction of the muscles in the vicinity.

Two forms of wry neck, the spastic or fixed form and the chronic or intermittently spasmodic form, are generally recognized. The chronic form, caused by myogenic contraction beginning usually in the sternocleidomastoid muscle and later involving other rotators, results in a peculiar nodding and rotating posture of the head. This is especially a disorder of adults.

In physiologic torticollis the pathology is not confined to the sternocleidomastoid. Examples of this condition are the cases resulting from eye strain, occupational attitudes, and habits. Extreme myopia causing monocular vision may be the source of a more or less permanent torticollis.

Acute torticollis may result either from what are presumed to be the effects of cold or muscular rheumatism ("stiff neck") or from some

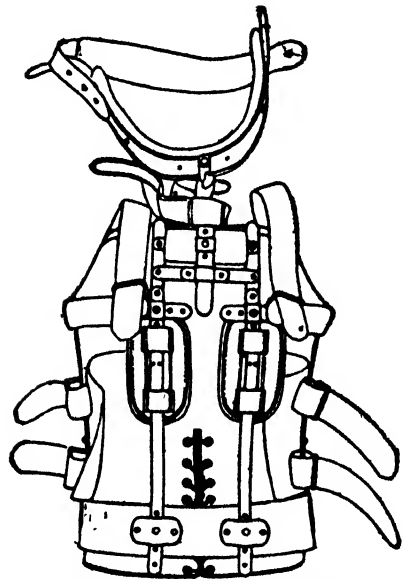
source of local nerve irritation which is not of sufficient duration to cause chronic wry neck. Slight fever may attend the onset in acute cases.

PATHOLOGY.—At times the lesion begins as a myositis induced by trauma. This results in shortening, which is more marked in the sternocleidomastoid because of the presence normally of a large amount of tendinous fibers in this muscle. Secondary changes occur in other muscles because these muscles—the rotators—overfunction in an attempt to relax the sternocleidomastoid. If the condition is present a long time, changes occur in bones, with asymmetry due to unequal development on the two sides.

TREATMENT.—If the condition is seen early, **orthopedic appliances** alone may be tried. Severe cases, however, require both **operation** and orthopedic appliances.

In dealing with torticollis surgically, the open operation is to be preferred to the subcutaneous procedure. The patient is placed in the dorsal position, with a sand-bag under the occiput and the head drawn against the contracted muscle. Local or general anesthesia may be used. In adults, infiltration of the skin, subcutaneous tissue and the muscle at its insertion with 1 per cent. **novocaine** solution is recommended. After division of the skin and subcutaneous tissue, the muscle at its insertion is exposed and the sternal end divided first. If necessary the clavicular end is then divided also. If there is any question as to the exact location of the great vessels, the skin flap can be reflected upward, the margin of the muscle exposed, and the posterior surface of the muscle liberated by

blunt dissection. The muscle can then be divided on the finger without fear of injury to the vessels. The wound is closed with interrupted sutures of plain catgut in the subcutaneous tissue and of horse hair in the skin. Mikulicz advises the **resection of the lower two-thirds of the sternocleidomastoid** in confirmed cases. This is done through an incision along the anterior border of the lower



Torticollis apparatus. (G. G. Davis.)

two-thirds of the muscle, which is divided near its insertion and reflected upwards.

Following the operation the head is fixed in the desired position by means of a **plaster-of-Paris dressing** for several weeks. **Apparatus** of various types may be substituted. One advised by G. G. Davis is reported as giving excellent results (see illustration).

This apparatus consists of a vertical bar going down the back of the neck and fastened to a light chest-jacket. The upper end of the bar carries a cross-piece, which

winds around the occiput and ends above the ears. From the ends above the ears one strap goes across the forehead and another from side to side under the chin. By means of wrenches the back-bar can be bent either around on its axis or else backward or forward, and thus be adapted to the special case.

The treatment of the mild, temporary form of torticollis known as "stiff neck" consists of **hot applications**, *e.g.*, cloths wrung out of hot water; gentle **massage** frequently repeated, and the administration of **salicyl compounds** where a rheumatic element is suspected. In the more painful cases, some relief may be procured by providing support in the form of **pasteboard** molded to the part, padded, and fixed with adhesive plaster or a bandage, or of a thick, firm **collar of cotton** stiffened with adhesive plaster. In the more refractory type of case **potassium iodide** and **radiant heat** may be employed.

In persistent and severe spastic torticollis, a careful examination should be made for local inflammatory or other sources of nerve irritation amenable to treatment. In cases in which the distortion has been allowed to persist for weeks or months before applying for relief, however, effective support in the form of a **plaster jacket** and **jury-mast** will enhance the benefit from other measures by relieving spasm and discomfort and thereby restoring the depleted vitality of the patient.

In the minority of cases of congenital torticollis in which the child is brought for treatment in early infancy and the disorder is of but moderate degree, the condition may be overcome, according to Whitman, by systematic **stretching** of the contracted parts, several times a day, **massage** being simultaneously applied to the tissues of the neck. The infant's posture while sleeping or being carried is, in addition, to be so adjusted as to counteract the deformity.

In spasmodic torticollis, drugs such as **hyoscyamus**, **atropine** hypodermically, **cannabis** and the **coal-tar products** may be tried, but nearly always fail. In mild and recent cases, **massage**, **muscle training**, and occasionally, **supporting apparatus**, may prove beneficial. In the severe, established cases, however, **resection of the spinal accessory nerve** as it enters the sternocleidomas-

toid, $1\frac{1}{2}$ inches below the tip of the mastoid process, has proven to be the only procedure from which results may reasonably be expected. Such resection has been found not to have any disabling effect as regards support of the patient's head. Where muscles other than the sternomastoid are involved, however, neurectomy will have to be performed also on the nerves supplying these muscles. Again, if there is permanent contraction of the muscles, irrespective of their innervation, complete **division of the muscles** may also be necessary. In a few cases cure has been attained by simple **stretching of the spinal accessory nerve**.

TUMORS.

Tumors of muscle are, in general, rare, although fibromata occurring in the rectus abdominis in women who have borne children are not uncommon. Carcinoma appears only in the form of secondary growths. Probably the most frequent seat of carcinoma is in the lower recti, as a result of the implantation of cells following operation for vesical carcinoma. Sarcomas are more frequently seen, but even these are uncommon. We have observed them in the body of the trapezius and gastrocnemius, and they are said to involve more frequently the sternocleidomastoid. They arise from the intramuscular connective-tissue, and may be of the round-cell, spindle-cell, or mixed variety. It is worthy of note that while tumors in bone are apparently preceded by trauma, tumors in muscle the result of trauma are rare—with the exception of the ossification which sometimes occurs. A tumor in muscle can be recognized early by the fact that it is displaceable when the muscle is relaxed but becomes fixed when the muscle contracts.

TREATMENT.—Benign tumors should be **excised**. Secondary carcinoma and sarcoma of muscle should

be treated by **radium**, imbedded first in the periphery and later into the substance of the growth. This may be supplemented by the **X-ray** or, in selected cases, by **excision**. If operation is carried out radium should be implanted at the time of the operation.

JOHN O. BOWER,
Philadelphia.

MUSK.—Musk (*moschus*) is the dried secretion from the preputial follicles of *Moschus moschiferus*.

Musk is expensive and very frequently adulterated. It occurs as irregular, brownish grains contained in an oval sac about 2 inches in diameter, smooth on one side, and covered on the other (outer) side with bristle-like hairs arranged concentrically around a central orifice. Each sac contains from 10 to 40 Gm. of musk.

The odor of musk is most penetrating, causing nausea in some individuals, and even headache and spasm in especially sensitive subjects.

PREPARATIONS AND DOSE.—

Musk is not official. The following 2 preparations were formerly recognized:—

Moschus, U. S. P. IX (musk), of which from 50 to 75 per cent. is soluble in water, forming a deep-brown, faintly acid, and strongly odorous solution. Dose, 2 to 5 grains (0.12 to 0.3 Gm.) by mouth, in pill or emulsion, or 20 grains (1.3 Gm.) when given in starch water by the rectum.

Tinctura moschi, U. S. P. IX (tincture of musk), of 5 per cent. strength. Dose, ½ to 1 fluidram (2 to 4 c.c.).

PHYSIOLOGICAL ACTION.—Musk has been credited with possessing a peculiar action in the relief of collapse and general vital depression. It has also been considered to act, under certain circumstances, as a nervous sedative. How these effects are produced is not explained by the data at hand. No experimental evidence of any distinct action has been forthcoming to support its clinical use; a psychic effect might, however, readily be conceived to occur under certain circumstances.

THERAPEUTICS.—Musk has been thought useful as a stimulant and antispasmodic, especially where **trismus** or

other spasmodic conditions complicate **acute febrile disorders**. When the strength of the patient is failing and there are manifest such symptoms as **subsultus tendinum**, muttering **delirium**, etc., rectal injections of musk, 10 grains (0.65 Gm.) to a pint (500 c.c.) of starch-water, have been recommended. Crookshank specified that musk was of benefit in acute infection where the symptoms were due to the intense action of toxins on the central nervous system, death appearing likely from their action on the medulla. In **pneumonia** the drug was often employed by Trousseau to sustain the patient through the critical period.

In spasmodic disorders, such as **hiccough** and **laryngismus stridulus**; in the persistent **spasmodic cough** that follows **pertussis**, and in **flatulence** musk employed in the form of the tincture is stated to have shown at times remedial power.

W. and S.

MUSTARD.—Mustard, as employed in medicine, is the flour of the seeds of either black mustard (*Brassica nigra* or *B. juncea*) or white mustard (*Sinapis alba*), the former of which is official. Their activity depends upon a volatile oil containing *allyl isosulphocyanide* (isothiocyanate) [C_3H_5-CNS], which, while not existing as such in the seed, is developed from the glucosid *sinigrin* (potassium myronate) through the agency of the ferment *myrosin* when mustard is moistened with water.

[The war "gas" known as "mustard gas," while also an oily fluid, is chemically dichlorodiethyl sulphide, $S(C_2H_4Cl)_2$, and is not related to mustard oil.]

PREPARATIONS AND DOSE.—

Sinapis nigra, U. S. P. (black mustard), consists of deep red-brown, sometimes gray-tinted seeds, with a powerfully irritating odor on crushing and moistening, and a strongly pungent and acrid taste. Dose (emetic), 2½ drams (10 Gm.).

Emplastrum sinapis, U. S. P. (mustard plaster), a uniform mixture of powdered black mustard (deprived of its fixed oil) and a solution of rubber, spread on paper, cotton cloth, or other fabric. Each 100 sq. cm. of plaster is officially required to contain not less than 2.5 Gm. of black mustard deprived of its fixed oil. When moist-

ened thoroughly with tepid water and applied to the skin, it produces decided warmth and reddening of the skin within five minutes.

Oleum sinapis volatile, U. S. P. (volatile oil of mustard), is obtained from black mustard by maceration and distillation, and yields not less than 92 per cent. of allyl isosulphocyanate. It is colorless or pale yellow, limpid, has an extremely pungent and acrid odor and taste, and is miscible with alcohol. Dose, $\frac{1}{8}$ minim (0.008 c.c.).

PHYSIOLOGICAL ACTION.—Oil of mustard diffuses readily in the tissues, and is therefore capable of causing a deep-seated irritation without actually destroying the more superficial skin strata. The liberation of the oil from mustard is rather slow, and it should therefore be removed from the skin somewhat before the required degree of local irritation has been secured.

UNTOWARD EFFECTS AND POISONING.—Mustard burns or irritations are slow in healing. A mixture of lime water and olive oil in equal parts will hasten resolution.

Kolb reports the case of a woman who had taken 6 teaspoonfuls of mustard internally for stomach pains. The next day she was unconscious, cyanotic, with small, irregular pulse (116) and contracted pupils. Respiration was almost arrested—only 3 or 4 to the minute—and of the Cheyne-Stokes type. The urine drawn by catheter was scanty and contained 5 per cent. of sugar and a trace of albumin. On the following day the patient was well, except for an intense general itching of the skin.

THERAPEUTICS.—As an emetic, mustard—1 dessertspoonful stirred into a glass of water—is used when, as in cases of poisoning, rapid emesis is required.

As a rubefacient and counterirritant, mustard is useful, mixed with flour or some other inert substance to limit its irritating action in myalgia, neuralgia, sciatica, inflamed joints, colic, pain in the chest in pulmonary tuberculosis, etc. A mixture of 1 part of mustard (English) to 4 of flour for adults, and of 1 to 6 for children and women with delicate skins,

generally proves sufficiently irritating. The mixture should be made into a rather thin paste with cool (not hot) water, vinegar, or white of egg, and spread evenly between two layers of muslin. The official mustard paper is a convenient substitute, but it is too strong for children. It is usually left in contact for one-quarter to one hour. To render the action milder, linen may be interposed between the skin and plaster.

Mustard may be used for the relief of pain in headaches of all kinds, and in gastric disorders mustard applied in a paste over the organ, just below the end of the sternum.

Mustard foot-baths are useful in the incipient stage of a great variety of disorders, while mustard sitz-baths are helpful in delayed menstruation. The latter baths, however, should not be made strong, the delicate mucous membrane of the vulva being easily irritated. In pulmonary edema complicating pneumonia a hot mustard foot-bath is recommended. Troublesome cough in epidemic influenza, croupous pneumonia, exudative pleurisy, pulmonary tuberculosis, and acute bronchitis is greatly benefited by the external use of mustard. In adults the mustard may be mixed with an equal amount of wheat flour or other meal; in children the dilution should be greater. Plasters may be placed on the chest and back alternately. Relief from cough in pulmonary tuberculosis is, in some cases, procured by the application of a mustard plaster over the trachea or bronchi (King). In pneumonia, influenza, and acute bronchitis a mustard plaster was found by Gorodtsoff a good substitute for morphine or other narcotics.

Heubner considers the mustard pack to exert a very useful revulsive effect in bronchopneumonia in children, dyspnea being relieved, cough lessened, and the work of the heart facilitated. He wrings out a large cloth from a mixture made by stirring 2 handfuls of mustard in a quart of hot water, and envelops the child to the neck in it for twenty minutes. A simple warm-water pack is then substituted for two or three hours. Sweating having occurred, a lukewarm bath, followed by a cool shower, is given, and the

child left quiet in bed for twelve hours. The interval between successive mustard packs should not be less than twenty-four hours.

W. and S.

MYALGIA. See RHEUMATISM, MUSCULAR.

MYASTHENIA GRAVIS. See MUSCLES, DISEASES OF.

MYASTHENIA PSEUDOPARALYTICA. See MUSCLES, DISEASES OF.

MYCOSIS FUNGOIDES.—DEFINITION.—Mycosis fungoides (granuloma fungoides; inflammatory neoplasms; lymphodermia perniciosa; multiple sarcoma cutis; sarcomatosis generalis; Alibert's disease) is a chronic, progressive, malignant skin affection, characterized primarily by an eruption of an urticarial, eczematoid, or lichenoid appearance and later by ulcerating fungoid tumors, and having a fatal termination.

SYMPTOMS.—The primary manifestations, or premycotic stage, may occur on any part of the body in the form of patches resembling those of erythema, eczema, psoriasis, lichen, urticaria, or pityriasis rubra. These lesions continue without much change for a period ranging from a few months to several years. In the second (mycotic) stage the lesions are seen to be raised above the surface and have a glistening aspect and a deep-red color. Papules as large as a pea develop, some of which disappear for a time, and then reappear. They may disappear from one region entirely and fresh ones appear elsewhere on the body. This stage may persist for months or years. The lesions give rise to much pain and itching. After a varying time well-marked tumors form, at first on the trunk, later on the extremities, either from a coalescence of adjacent papules or by new formation, hemispherical, oval, or irregular in outline, sometimes pedunculated, bright or dark red in color, and either hard or soft in consistency. In this stage large patches of infiltration may be present. The epidermis becomes thinned and glistening. Tumors may be observed in different phases of evolution or retrogression. Some undergo resolution and are absorbed; others ulcerate and

form a fungous mass. During the progression of the disease the tumors may develop all over the body, and may involve mucous membranes, appearing upon the tongue, palate, and larynx. In this stage the pain and itching usually diminish, but painless enlargement of the lymphatic glands appears.

Though the general health may remain unaffected for a long time, a condition of marasmus develops and the patient dies from an attack of diarrhea, from pulmonary complications, or from septic infection. The disease is fortunately a rare one, and it almost always has a fatal termination.

DIAGNOSIS.—Clinically, mycosis fungoides, in the early stage, stimulates the various affections already mentioned. From the common forms of erythema it may be distinguished by the sharply defined limit of its patches. From eczema it may be differentiated by the persistence of its lesions. From psoriasis it differs in the unusual location and unusual chronicity of its lesions. While the evolution, retrogression, and fungous appearance of the tumors would indicate this disease, the new growths themselves might be confounded with sarcoma, but it must be recollected that in sarcoma the lymphatic glands do not suffer enlargement, nor do the neoplasms often disappear by resolution.

Histologically, mycosis fungoides may be confounded with the granulomata of tubercle and syphilis, the sarcomata, and the leukemic and pseudoleukemic growths of the skin. It resembles syphilis in many particulars. It differs from cutaneous tuberculosis in that giant cells with central caseous degeneration do not occur. In the skin lesions of leukemia the vessels of the cutis are affected with marked edema and there is active diapedesis from them, with subsequent infiltration of the adjacent cutis with leucocytes; simply a leucocytic infiltration without marked fixed-cell proliferation, mitosis, or imperfect giant-cell formation, as is seen in mycosis fungoides. Pseudoleukemia cutis resembles syphilitic granuloma more than mycosis fungoides.

ETIOLOGY AND PATHOLOGY.—Mycosis fungoides is believed to be an

infectious granuloma, probably due to a microparasite (Schamberg). Galloway and Macleod have found that in the pre-fungoid stage there is a connective-tissue-cell proliferation around the blood-vessels of the subpapillary and papillary layers, the hair follicles, sebaceous glands, coil ducts, and occasionally the coil glands, and forming foci independent of these structures among the connective-tissue bundles. In the epidermis active mitosis of the prickle cells and downgrowth of the interepithelial processes were noted; also nests of corium tissue in the mucous layer and interepithelial edema going on to the formation of reticular spaces. To the tumor stage the cell proliferation increases, and the cells show a marked tendency to break down, shown by the crenation, irregularity, and fragmentation of the cells. The granuloma encroaches on the downgrowing epithelium, flattens it out, spreads up to the surface, and is covered only by a layer of the stratum corneum.

TREATMENT.—The itching of the early stage is to be relieved by applications of antipruritic remedies in proper dilution. Pain may require the use of morphine.

Arsenic, hypodermically, has been found beneficial by Köbner. The general condition should be kept as favorable as possible through administration of **tonics** and **good food**.

Local applications of **ichthyol**, **pyrogallol**, **resorcinol**, **camphorated naphthol**, and injections of **phenol** have been used. The ulcers are best dressed with antiseptics, such as **iodoform**, **acetanilide**, **iodol**, **europhen**, **thymol iodide**, **bismuth subiodide**, etc. Cleanliness of the entire skin surface should be maintained. Persistent **purgation** was apparently the cause of recovery in 1 of Crocker's cases.

The most efficient remedy is the **X-ray**; it is most effective when applied early in the disease; in the later stages it apparently merely controls the process during the time of its use. The itching is often greatly relieved by it.

Rapid disappearance of the lesions under the rays has been known to induce a pronounced toxemia, apparently responsible for death in one of C. J. White's cases;

careful attention to dosage is therefore required.

Case in which small doses of **calomel**, **betanaphthol** and **liquid paraffin** improved the itching, and high **rectal douches**, the general condition. **Diet**, **collosol sulphur** internally and **sunbaths** were also used. *B. coli autogenous vaccine* cleared up the premycotic skin symptoms. Ulcerative tracheal involvement eventually caused death. Wills and Hadfield (Brit. Jour. of Derm., Mar., 1925). W.

MYELITIS. See SPINAL CORD, DISEASES OF.

MYOCARDITIS. See HEART AND PERICARDIUM, DISEASES OF.

MYOMA. See OVARIES AND FALLOPIAN TUBES, and UTERUS.

MYOPIA.—This term is applied to the partial closure of the lids to render vision less indistinct, by narrowing the circles of diffusion on the retina: an action of which myopes generally learn the benefit.

DEFINITION.—That error of refraction in which the principal focus of the dioptric surfaces lies in front of the retina. Rays parallel when they enter the eye come to a focus in the vitreous, and diverge again, forming a circle of diffusion upon the retina. The eye is too long anteroposteriorly, as compared with the curve of its surfaces.

SYMPTOMS.—The elongation of the eyeball may be part of its general enlargement in all directions, and in any case makes the front of the eye prominent, so that it looks large. In high myopia this elongation is very evident when the eye is turned strongly toward the nose. The pupil is often large and the anterior chamber deep. The expression of the patient is likely to be rather vacant. He is unable to perceive much of the facial expression of others,

and hence does not learn to respond to it by facial movements of his own. All distant vision is indistinct; the myopic child, therefore, is at a disadvantage in many games, and is inclined toward reading and other amusements requiring only distinctness of near vision. The constant effort to bring the eyes near to the object looked at is likely to cause an habitual stoop.

Myopia of high degree is mostly attended by divergent strabismus. The elongation of the eyeball makes it very much harder to turn in its socket, and the limiting of the range of distinct vision to a near point compels the myope to converge his eyes to a greater extent and to converge them more constantly than if normal. As the myopia increases, this need and difficulty of convergence increases, until the effort becomes too great to be habitually sustained, binocular vision is given up, and the worse eye allowed to squint. The process of elongation of the eyeball is, in the vast majority of cases, distinctly pathological and attended by changes in the coats of the eye, especially by disturbance and atrophy of the choroid in a crescentic area at the temporal side of the optic disk: the so-called myopic crescent. In high myopia the vitreous humor usually shows opacities and may be abnormally fluid, the crystalline lens is liable to become partly opaque, and the retina often becomes detached. Distant vision is always worse than near vision; but the latter may also be very imperfect. Headache is not usually present. But excessive efforts of convergence may give rise to headache, vertigo, or the inflammatory symptoms of eye-strain.

DIAGNOSIS.—Myopia is recognized and measured by: the improvement of vision by concave lenses, the

weakest lens giving the best distant vision being the measure of the myopia; the blurred image in the direct method of ophthalmoscopic examination, rendered clear by a concave lens which corrects the myopia, and the reversal of movement by skiascopy, the distance of the point of reversal from the eye being the focal distance of the correcting lens.

ETIOLOGY, PATHOLOGY, AND VARIETIES.—Myopia may be due to excessive curvature of the cornea, or crystalline lens,—*myopia of curvature*,—or to an increase of refractive power in the lens substance,—*index myopia*; but the great majority of cases are due to elongation of the eyeball,—*axial myopia*. Myopia is often observed temporarily for a few weeks or months after an attack of iritis or iridocyclitis,—*inflammatory myopia*. This last is probably due to alteration of curvature in the lens, although an alteration of index has been suggested. Prior to senile or diabetic cataract myopia may develop, probably by increased refractive index of the lens nucleus, or diminished index of refraction in the lens cortex. This change enables old people who have previously required convex lenses to read without them, and is therefore called "second sight." It is but a temporary benefit, and not an unmixed good. To the extent that near vision is gained distant vision is lost, and both are lowered by the haziness of the crystalline lens.

The mass of cases of myopia develop in eyes, not myopic at birth, from excessive strain of near-seeing. Heredity, bad hygienic surroundings, and impaired general health are predisposing causes. But the efficient exciting cause is excessive near work for the eyes.

During near vision the eye muscles are actively innervated, and the eyeball compressed laterally between them, so that there is a constant tendency to force it to elongate. The condition of congestion of the choroid and inflammatory softening of the sclera, that develops under excessive use of the eyes for near work, causes the sclera to give before the intraocular pressure, and permanent change in the shape of the eyeball results. As myopia increases, distant vision becomes less perfect, the range of clear vision more restricted, the efforts of convergence of the eyes greater and more constant, and at the same time the sclera is thinned by distention and less able to withstand the pressure of its contents. In this way the myopia tends to go from bad to worse, becomes *progressive*, and when this progress has become so great that it cannot be checked it is said to be *malignant myopia*.

The idea has sometimes been entertained that use of the accommodation tended to increase myopia by increasing the intraocular tension; but this is directly disproved by both clinical and experimental studies of the subject. Many hypotheses have been advanced regarding myopia without any sufficient basis of facts, namely: that heredity acted by determining the proportions of the cranium or the shape of the orbits, or that a special diathetic or vascular condition was the chief determining factor in the case. Levinsohn has made the suggestion that gravity causes elongation of the eyeball when stooping forward. This view he supported by experiments on monkeys, which were suspended with the head downward until myopia seemed to result. The large number of myopic eyes that also exhibit considerable astigmatism make

it probable that strain of the eyes from astigmatism, causing choroidal disturbance and scleral softening, is an important factor in many cases.

TREATMENT.—Myopia should be corrected by **concave lenses**, which should be worn constantly. For young persons the **exact optical correction** should be worn all the time, although in rare cases it may be better to use a weaker lens for a time for near work. Presbyopes will always require, for near seeing, a lens sufficiently weaker to make up for their presbyopia. The correcting lens gives the myope distinct vision and the visual range of the emmetropic eye, and places the check of accommodative effort upon the tendency to excessive convergence. Correcting lenses may be unsuitable for those cases in which binocular vision, and therefore strain of convergence, have previously been given up; or where the vision is so imperfect, or the minifying effect of the correcting lenses so great, that objects will still be held close to the eye to gain the benefit of larger retinal images.

The incomplete correction of myopia, unless the glasses are so weak as to be of no material benefit, is extremely dangerous. By looking through such lenses obliquely the myope soon finds that he can see farther and more distinctly than by looking squarely through them, and he soon falls into the habit of looking obliquely. By looking obliquely through a lens the pencil of rays received by the eye is rendered astigmatic, and the evils of high uncorrected astigmatism are thus entailed. When the **full correction** for the myopia is worn, looking obliquely through the lenses makes vision worse and is instinctively avoided.

The wearing of correcting lenses en-

ables the myope to reduce his efforts of convergence to nearer the normal. But there still remains the increased difficulty of turning an elongated eye in its socket. To help still farther, the amount of **near work** required of such eyes must be **limited**, and surrounded with the most favorable conditions, including the use of the **best illumination** and a **correct posture**, with **frequent interruptions** during which the **eyes are permitted to rest on distant objects**. These precautions are of the greatest importance during childhood and adolescence, when myopia begins and shows the most general tendency to increase.

Operation.—The surgical treatment of myopia by **removal of the crystalline lens** is appropriate for a few cases of very high degree—15 D. and upward—in which correcting lenses give unsatisfactory results although the eyes are capable of good vision. In children the removal is to be effected by a small discission of the lens, repeated several times, if necessary, until the absorption of the lens substance leaves a clear pupil. In adults the lens may be extracted after a preliminary small discission to render it opaque. The operation is quite as formidable and dangerous as that of the removal of the opaque lens,—cataract. (See Volume III.) The removal of the crystalline will generally correct about 18 D. of myopia, and the higher the myopia, unless it be due to increased curvature of the cornea, the greater will be the effect of the operation. The removal of the crystalline also gives a larger retinal image than can be obtained through concave correcting lenses, with a correspondingly superior acuteness of vision. In cases suitable for this

operation such improvement should amount to 50 or 60 per cent. After removal of the crystalline, although the patient is much less dependent on his glasses, they will still be necessary to secure the best vision, and different lenses will be required for near and far seeing, on account of the loss of all power of accommodation.

EDWARD JACKSON,
Denver, Colo.

MYOSITIS. See MUSCLES, DISEASES OF.

MYRRH (myrrha) is a gum-resin obtained from *Commiphora myrrha*. It is official in all pharmacopeias. Official myrrh is collected by the Somalis in northeastern Africa, partly from natural fissures and partly from incisions made for the purpose. It is first yellowish white, but as it hardens it becomes darker and finally of a reddish-brown color. It occurs in irregular, more or less rounded nodules or tears, from 2.5 to 10 cm. (1 to 4 inches) in diameter. It contains from 2 to 5 per cent. of a volatile oil, which imparts to it its characteristic odor. A resin constitutes from 25 to 50 per cent. of myrrh. The remainder is largely gum. Myrrh has a balsamic, aromatic odor and an aromatic, bitter and acrid taste.

PREPARATIONS AND DOSE.—*Myrrha*, U. S. P. (myrrh), forms a brownish emulsion when triturated with water. Dose, 8 grains (0.5 Gm.).

Tinctura myrrhæ, U. S. P. (tincture of myrrh), is a 20 per cent. preparation. Dose, 30 minims (2 c.c.).

Myrrh is also contained in the following compound preparations:—

Pilulæ rhei compositæ, N. F. Dose, 2 pills.

Pilulæ aloes et myrrhæ, N. F. Dose, 2 pills.

Tinctura aloes et myrrhæ, N. F. Dose, ½ fluidram (2 c.c.).

Tinctura capsici et myrrhæ, N. F. (hot drops). Dose, ½ fluidram (2 c.c.).

Tinctura antiperiodica, N. F. (Warburg's tincture). Dose, 1 fluidram (4 c.c.).

Mistura ferri composita, N. F. IV (Griffith's mixture). Dose, 4 fluidrams (16 c.c.).

THERAPEUTICS.—Myrrh has astringent, carminative, antiseptic, and possibly emmenagogue and expectorant properties. Locally, the tincture of myrrh, as such or diluted, is a useful application to **spongy gums**, in **aphthous stomatitis**, and to **indolent ulcers**. It has been used internally, with asserted benefit, in the later stages of **bronchitis**, in **chronic cystitis**,

and in the **leucorrhœa** of **chronic metritis**. In **scurvy** the administration of teaspoonful doses of tincture of myrrh mixed in with some astringent infusion or decoction has been recommended. W. and S.

MYXEDEMA OR PROGRESSIVE HYPOTHYROIDIA. See THYROID GLAND, DISEASES OF.

N

NAILS, DISEASES AND INJURIES OF THE.—Besides the implication of the nail in general morbid processes—such as syphilis, neuritis, leprosy, etc.—there are several strictly local diseases that require special notice.

ATROPHY.

Atrophy of the nail (*atrophia unguium*; *onychatrophia*), either congenital or acquired, is characterized by a decrease in size or thickness, splitting, crumbling, softening, and discoloration. In the congenital form the nails may be absent, distorted, or defective. Acquired atrophy may be caused by any general or local disturbance affecting the matrix, as traumatism, syphilis, fevers, etc. The nail may become smaller and thinner, flexible and easily broken, or soft, granular, and present a worm-eaten appearance. The surface of the nail may be smooth and normal in appearance, or may be discolored, opaque, or yellow and fissured.

The white spots often observed on the nails (*leuconychia*) are an indication of subnormal vital energy, the result, often, of exhausting disease, dissipation, sexual excesses, overwork, or worry.

TREATMENT.—The first indication is to remove the cause if possible. If the diseased nails are painful or interfere with the patient's work, the use of **soothing ointments**, and the application of **wax, gum, or flexible collodion** on the nails as a protective covering, will afford relief. The subsequent use of **oils and ointments** applied over the nails will improve this condition.

If this prove insufficient, **acid nitrate of mercury** must be used after anesthetizing

the parts with a 10 per cent. solution of cocaine. Such an application may also be rendered painless, according to Randolph, by saturating **nitric acid** with the **cocaine hydrochloride**.

The nail groove may be **excised** and the **matrix scraped**, or the nail may be **removed** and the remaining ulcer dressed with powdered **lead nitrate**, **iodoform**, **iodol**, **thymol**, **iodine**, **aristol**, or **europhen**—**constitutional treatment** is demanded in all cases.

HYPERTROPHY.

This affection (*hypertrophia unguium*; *onychauxis*), usually ascribed to pressure, is characterized by an increase in the length, breadth, or thickness of the nail, and may be either congenital or acquired, idiopathic or symptomatic (as in eczema, psoriasis, syphilis, ichthyosis, etc.). There may be simple enlargements, without change in quality or texture, or there may be structural changes, the nail becoming roughened, furrowed, or opaque, and in some cases of a yellowish-brown or black color.

If the growth is lateral, inflammation of the surrounding tissues (*paronychia*) may ensue, or it may cause inflammation of the matrix (*onychitis*). When the nails become curved and claw-like the condition is called *onychogryphosis*.

Though the growth is very gradual, pressure upon the underlying tissues causes local disorders, especially if the nail cracks, when painful inflammatory symptoms follow. It produces heat and discomfort when affecting the feet, shoes being worn with difficulty. When the nails of the hands are the seat of the

hypertrophy such a condition constitutes quite a deformity.

TREATMENT.—The overgrowth should be filed down or sawed. In other words, measures tending to give the nail its normal shape should be resorted to. All complications are of the nature of those attending the so-called "ingrowing toe-nail," and the treatment given for the latter condition (see below) is also applicable.

NUTRITIVE ALTERATIONS CAUSED BY DISEASE.

ECZEMA.

Ecze^ma produces the most frequent examples of nail disease. The changes may occur on the nail walls, matrix bed, and plate, and are brought about by the etiological factors of the primary disease. Generally appearing after the age of 20, it continues throughout adult life.

In the acute form the nail walls are red and swollen, the plate becomes more convex, rough, lusterless and discolored, and soft spots occur in it, which become minute punctate depressions. Pain is felt in the bed.

In the subacute and chronic forms the nail may be the seat of transverse depressions or ridges, vertical ridges, hyperkeratosis of the bed, with increase in the convexity of the plate and, later, a disappearance of the granular detritus, and thinning of the plate with increased brittleness, exfoliation of the surface cells of the plate, leuconychia, or final loss of the nail. A deep, transverse furrow may result, if the matrix is affected.

TRAUMA OR FELON.

When the matrix is unaffected by these accidents, or when they are slight, the nail-changes are insignificant. When the matrix is involved a permanent change occurs that is indefinitely reproduced. These constant deformities are transverse depressions, vertical ridges, hyperkeratosis subungualis and its sequelæ, and discoloration. Less often the changes are round punctate depressions, atrophy, exfoliation of plate surface, increased convexity, brittleness, opacity, koilonychia (spoon-nail), gryphosis, leuconychia, transverse ridges, vertical depressions, invasion of air into the plate, and subsequent crumbling or entire loss of the nail.

PARONYCHIA.

This is an inflammation of the tissues around the matrix and occurs usually in washwomen or scrubwomen and in those who subject their fingers to constant irritation. In these cases the nail becomes discolored and the seat of transverse depressions and hyperkeratosis subungualis; there is a lifting of the plate which allows the keratotic granules to leave the bed, leaving a flat, horny floor covered by a thin, dome-shaped roof.

TREATMENT.—A pledget of cotton should be packed in between the nail and the soft parts, the imbedded portion of the nail having been previously excised.

In early paronychia, the writer pushes a fine sterile probe or blunt end of a needle under the cuticle and lifts the latter gently up, often liberating a few drops of pus. A fine narrow ribbon of sterile rubber is now pressed in, sterile vaselin applied, and a square of rubber tissue with a small hole placed over the end of the finger, followed by moist gauze and a short finger splint. The patient keeps the dressing wet with warm salt solution. Repetition for 2 or 3 days may cure, obviating removal of the nail. Coues (Boston Med. and Surg. Jour., Nov. 5, 1925).

PSORIASIS.

Psoriasis of the nails occurs oftenest in men between 20 and 40. The most frequent (57 per cent.) lesion is hyperkeratosis of the bed, with its subsequent changes. Discoloration and transverse depressions occur in about 38 per cent. of the cases. Less frequently found are simple hyperkeratosis subungualis, brittleness of the plate, thinning, opacity, vertical ridges, exfoliation, increased convexity, etc. (White). The psoriatic papules form on the bed, raise up the plate, and allow the air to enter the plate cells, producing opacity and discoloration.

DERMATITIS PROFESSIONALIS.

These cases are due to some noxious occupation, or an accidental poisoning of the skin. White noted the presence of koilonychia in 40 per cent. of his cases and mentions as other changes round punctate depressions, discoloration, transverse depressions, vertical ridges, and

hyperkeratosis subungualis, with its sequelæ.

SYPHILIS.

This is not a common affection of the nails. When the nail wall is the seat of primary chancre, a series of parallel transverse depressions, with or without discoloration, develops, or the plate may ulcerate and drop off.

In the secondary stage the disease may be characterized by the formation of a papule on the bed, or by a general, moist elevation of the nail.

The tertiary lesion is usually a dry one; white punctate depressions form in vertical series at the root of the nail and there is hyperkeratosis of the bed or a thickened, yellow, crumbling plate.

TINEA TRICHOPHYTINA.

This condition (onychomycosis; ringworm of the nails) is a very rare one. It is caused by *Tinea megalosporon*, and appears first at the distal portion of the nail, gradually spreading backward. The megalosporon first attacks the bed, producing opacity and a discoloration of the plate, at first whitish yellow, later brown, or even black. With the progressive darkening color the bed becomes increasingly hyperkeratotic; the plate is raised more and more from the bed and exhibits transverse depressions or elevations, or vertical ridges; the plate becomes roughened upon the surface, exfoliates, atrophies or splits, and becomes loosened. Chronicity marks this disease. Under proper treatment two years are necessary for its cure, while, untreated, it may endure actively for thirty years. Ringworm elsewhere on the body may aid in the diagnosis, which is otherwise difficult.

TREATMENT.—Soften the nail with a solution of potassium hydroxide, remove as much of the diseased portion as possible, and keep the remainder covered with a 10 or 20 per cent. ointment of mercury oleate until the entire diseased area exfoliates or is replaced by new and healthy growths. Solutions of mercury bichloride, and of creosote, and the oleates of copper and tin are also useful (Shoemaker).

TINEA FAVOSA.

This affection (tinea favosa unguium; onychomycosis favosa), though rare, is

more common than ringworm, and its appearance is similar to the latter. It is caused by *Achorion schönleinii*, which attacks the distal end of the bed and causes an opacity and discoloration of the plate. As in ringworm, the hyperkeratosis spreads backward, and the plate, raised from its bed, becomes increasingly darker, even black, and transverse depressions or ridges appear on its surface. When the plate is attacked it assumes a honey-combed appearance, leading on to crumbling, splitting, and final exfoliation of the nail. This affection in its course and treatment resembles that of ringworm.

NUTRITIVE ALTERATIONS IN OTHER DISEASES.

The pallor of the nails in anemia and chlorosis; their lack of luster in syphilis and gout; the subungual hemorrhages in scurvy, and the subungual ecchymoses in diabetes; the development of furrows, fissures, and ridges in chlorosis, Morvan's disease, cyclical insanity, rheumatism, typhus, typhoid, and relapsing fevers, and after seasickness, nervous exhaustion, and scrofulosis; the shedding of nails in diabetes, locomotor ataxia, alopecia, hysteria, fevers, and small-pox; the talon-like nails of Morvan's disease; the hypertrophied nails of acromegaly; the enlarged, horny nails of scrofula, and the thick, curved, clubbed nails of tuberculosis are well-known conditions.

CONTUSION.

Contusion of a nail by a blow, a compression, etc., is a common occurrence. Unless sufficient to cause destruction of the matrix, the result of such an injury is usually slight, the acute pain quickly disappearing; in some cases a subungual hematoma is formed. When, however, the traumatism is serious and the nail is torn off, severe suffering is induced, which may persist a long time. Again, infection may occur, leading to inflammation and suppuration.

TREATMENT.—Slight cases of contusion require no treatment. After a few minutes the pain generally decreases, then ceases, and the ecchymosis that shows through the nail is generally eliminated through the growth of the nail.

In severe cases the finger or toe should be immersed in a hot saturated solution

of borax, then dressed with iodoform or orthoform if pain continues. The dressing should be changed every day where a toe is the seat of injury. If the nail is partly torn off, it should be carefully cleansed along with the underlying tissue, replaced, and retained with a bandage applied over the dressing.

ONYCHIA.

This is an inflammatory disorder of the matrix of the nail, popularly called a *run-around*, which may follow an injury such as that first described or the introduction between the nail and the underlying tissues of infectious matter, along with a foreign body (a thorn, a splinter, etc.). The finger-tip becomes warm and congested, and severe pain is generally present. An abscess is formed after a few days, the pus being evacuated through the aperture formed by the offending body. If none such exists, the nail may become softened and perforated. When the accumulation of pus is marked, there may be febrile and other symptoms denoting general involvement.

In the vast majority of cases, however, the symptoms generally become less marked and involution soon follows, sometimes after the loss of the nail. This is always replaced, though not always by as perfect a nail as the one shed.

TREATMENT.—The treatment indicated is by antiseptic methods that tend to destroy the infectious germs. **Hot-water baths**—as hot as can be borne—sometimes speedily arrest the process. **Alcohol** acts in the same manner. If a splinter or other infectious body have penetrated the tissues, the pus-cavity can usually be penetrated without pain with a hypodermic needle and washed out with a 1:5000 mercury bichloride solution. Bathing the finger in such a solution at frequent intervals, or, better still, leaving it therein an hour several times a day, sometimes arrests the infectious process early in its career. Whenever there is imprisoned pus, it should be liberated by an incision and the cavity washed out, using a hypodermic syringe. Incision into the flesh, according to Tousey, is always radically wrong, even though the pus be nearly a dram (4 c.c.) in amount. The attachment of the cuticle

to the dorsal or exposed surface of the nail should be separated by a **tenotome** to a sufficient extent to permit the escape of the pus and the introduction of a stick of **silver nitrate** to disinfect the sulcus. With this treatment there is no disfigurement. **Hydrogen dioxide**, diluted (1 part in 3), is very effective in such cases.

MALIGNANT ONYCHIA.

This is a complication of the disorder just outlined, which may occur in persons who are constitutionally weak or adynamic or in scrofulous or lymphatic children. It usually affects the index finger, the thumb, or the big toe, and is the active manifestation of a local ulcerative process in the matrix of the nail. The latter becomes brownish or black, and is shed, leaving underneath a granular fungous mass which shows no tendency to heal. The finger sometimes becomes enormously enlarged and discharges considerable fetid pus. Necrosis of the bone of the phalanx involved occasionally follows.

TREATMENT.—Proper active measures usually prove promptly effective. The nail should be removed with forceps. Pain may be prevented by first injecting a 4 per cent. solution of cocaine under the nail. The parts are then dressed with iodoform. A day or two later, after brushing the parts with a 4 per cent. solution of cocaine, the ulcerating area is touched with silver nitrate, burnt alum, or tincture of chloride of iron. This should be repeated, if need be, several times at two- or three-day intervals.

INGROWING TOE-NAIL (LATERAL ONYCHIA).

The term "ingrowing toe-nail" is applied to a condition usually confined to the great toe, in which the edge of the nail (almost always the outer edge) is forced into the adjoining soft parts. Swelling of the latter being induced, they overlap the nail, the point or line of contact becoming the seat of ulceration and granulations. It is usually due to the pressure of tight shoes, and is therefore generally met with in young adults. It is also frequently encountered in soldiers as the result of prolonged marching with heavy accoutrements that increase the pressure upon the feet. Lymphatic sub-

jects are more liable to it than others, and the affection is exceedingly persistent in them. It often accompanies diabetes and may occur as a complication of febrile diseases of long duration, fractures and other processes tending to debilitate the organism, hyperidrosis, etc., but most frequently as a result of badly shaped shoes.

TREATMENT.—In mild cases **broad-toed shoes** giving freedom to the toes, **frequent ablutions**, and finely powdered **sodium borate** (borax) or **tannic acid** applied to the dressed tissues usually suffice for a cure. The mere daily introduction of **cotton** under the **lateral edge** of the **nail**, by gradually raising the latter away from the soft parts, sometimes yields very satisfactory results. **Scraping** the **center** of the **nail** until it is quite thin occasionally suffices to relieve the pressure.

In the great majority of cases the ulceration requires active measures besides a change of footwear. The ulcerated tissues must first be relieved of their granulations. This can easily be done by using **tincture of ferric chloride**, **burnt alum**, **hydrogen dioxide**, powdered **lead nitrate**, etc., after anesthetizing the parts with a 4 per cent. solution of **cocaine**. Or, they may be scraped with a **curette** or gently **cauterized** with the **mitigated stick**, **zinc oxide**, and **silver nitrate**. This being done, a small piece of cotton-wool covered with **iodoform**, **iodol**, or **aristol** is gently inserted with a probe into the diseased cavity, the **soft parts** being **raised** away from the nail. These measures do not always procure a radical cure, however, particularly if the patients again use narrow or short-tipped shoes. In such cases **surgical measures** are preferable. The simplest of these is to anesthetize the tissues—or the patient—and, after careful cleansing of the parts, to simply **pare off** the **redundant tissues**, granulations and all, on a level with the edge of the nail. The nail-edge being then carefully trimmed, an **iodoform dressing** is applied. Or, the diseased parts may be **dissected out** and a plastic union obtained by a few stitches.

Another method is to apply a warm 40 per cent. solution of **liquor potassæ** to the portion of the nail to be removed. After

a few seconds the uppermost layer of the nail will be so soft that it can be **scraped off** with a piece of sharp-edged glass; the next layer is then moistened with the same solution and scraped off; this must be repeated until the remaining portion is as a thin sheet of paper, when it is seized with forceps, lifted from the underlying soft parts, and **excised**. This operation, according to Pürckhauer, is both painless and bloodless.

J. L. Andrews states that **plaster applied diagonally** around the toe in such a manner that the **soft parts** shall be **drawn away from the nail** without direct pressure over the latter is sometimes efficient in ingrowing toe-nail.

The older surgeons recommended an evulsion of the nail, an operation performed by forcibly inserting a scissors under the nail in the mesial line; but this is now condemned because the new nail is generally a malformed one and hypertrophy occasionally follows.

A number of other operations have been suggested. **Cotting** **removes** the **soft parts**, healthy and diseased, down to the margin of the nail. This is curative in many cases. **Anger** excises the diseased tissue and **removes half of the nail**. **Dowd** does a similar operation, but, in addition, **destroys** the **matrix** and closes the wound with stitches. Many good results follow these latter operations. **Keller** **splits** the **nail** in the **center** through the **matrix** down to the bone and **freed** the **matrix** and **lateral border** of the **nail** by an **incision** down to the nail, about $\frac{3}{16}$ inch from the lateral borders and extending back beyond its base. These **lateral borders** are **freed**, **elevated**, and **carried out** over the healthy tissue, and the **matrix** of the **elevated** portions is **removed**.

Van Meter **excises** a **diamond-shaped** piece of tissue, at the **side of the toe**, the incision being carried down to the periosteum, and **closes the wound by suture**. This draws the overlapping exuberant granulation tissue away from the nail.

T. L. Deavor **excises** a **V-shaped** section from the **root of the nail**, in the center, turning back the soft parts in all directions and exposing the limitations of the nail. The **nail** is **removed**, and, by **cutting** and **scraping**, the **nail-bed** and **matrix** are

cleared of all tissue down to the periosteum.

Melted candle wax poured into the crevice gives relief. Melville (Internat. Jour. of Surg., Jan., 1922).

NAPHTHALENE AND ALLIED COMPOUNDS.—Naphthalene (naphthalenum; naphthalin; white tar; tar-camphor; mineral camphor; "moth balls") is a hydrocarbon [$C_{10}H_8$] obtained from coal tar. It occurs in white scales or powder, with a burning, aromatic taste. It is soluble in alcohol, chloroform, and ether, the fixed and volatile oils, and acetic acid, but it is insoluble in water. It melts at 175° F. (79° C.), and volatilizes slowly at ordinary temperatures, more rapidly when heated. When ignited it is consumed, leaving no residue; its vapor burns with a smoky flame. It should not give any reaction on moistened blue litmus paper, and should dissolve in concentrated sulphuric acid, when warmed gently, without color.

DOSE.—*Naphthalenum*, U. S. P. VIII (naphthalene), may be given in doses of 2 to 15 grains (0.13 to 1 Gm.) in powder or in capsule. The official average dose is 2 grains.

PHYSIOLOGICAL ACTION.—Locally, in the human subject, naphthalene temporarily irritates the mucous membranes; this effect becomes more marked when the drug is dissolved in oil or alcohol. Naphthalene is an antiseptic, though, according to some, this property is less marked than in the case of its derivatives, alpha- and beta- naphthol.

Given experimentally in large amounts to the lower animals, naphthalene causes diarrhea and emaciation, the latter due either to disturbed gastrointestinal functioning or to the parenchymatous nephritis which is soon also induced. Peculiar changes in the eyes, including subretinal effusion, bright points or yellow plaques on the retina, atrophy of the optic nerve, and progressive clouding of the lens, have been observed, and, according to V. d. Hoeve, prolonged use of the naphthols in man may cause an incipient retinal degeneration. Being partly oxidized in the body, naphthalene appears in the urine as alpha- and beta- naphthol and naphtho-

quinone, all in combination with glycuronic and sulphuric acids (Cushny). A brownish discoloration of the urine may result from the presence of these substances and their derivatives.

UNTOWARD EFFECTS AND POISONING.—Otte, after ingesting 8 grains (0.5 Gm.) of naphthalene (subsequently found pure on analysis), suffered from abdominal pain, diarrhea, tenesmus, protracted vomiting, sharp kidney pains, and slow pulse, continuing to be ill for five days. Though perhaps a case with unusual idiosyncrasy, this result imposes some degree of caution in the use of large doses. An eruption simulating that of measles, and followed by desquamation, has also been observed after the use of naphthalene.

THERAPEUTICS.—The therapeutic value of naphthalene depends upon its antiseptic and antiparasitic properties.

As intestinal antiseptic it has been used, in 5-grain (0.3 Gm.) doses, with apparent benefit in **typhoid fever** (Wolff), in **acute** and **chronic intestinal catarrh**, in **fermentative diarrhea**, and in **cholera**. It diminishes the activity of the intestinal bacteria, as shown by C. Schrwald, who advises its use in conjunction with calomel. In **dysentery** 10 or 15 grains (0.6 to 1 Gm.) may be given in a warm decoction of althea (marshmallow) by rectal injection. In the **summer diarrhea** of children, $\frac{1}{6}$ to $\frac{1}{4}$ grain (0.01 to 0.015 Gm.) may be given every two to four hours.

Naphthalene in doses of 3 to 10 grains (0.2 to 0.6 Gm.), combined with castor oil and disguised with a couple of drops of oil of bergamot, is useful in treating **ascarides** (Mirowitch). **Seat-worms** (*Oxyuris vermicularis*) can be well treated by the injection of 10 or 15 grains (0.6 to 1 Gm.) of naphthalene in 2 or 3 ounces (60 to 90 c.c.) of oil into the rectum. Bosini even recommends the administration of 22 grains (1.5 Gm.), after purgation, preferably with calomel. Schmitz states the dose for children as ranging from $2\frac{1}{4}$ grains (0.15 Gm.) for a child $1\frac{1}{2}$ years old to 6 grains (0.4 Gm.) for one of 12 or 13 years. He first gives a purge, then 4 doses of naphthalene daily for two days; this is then repeated twice at weekly intervals. For **tape-**

worm, 15 grains (1 Gm.) should be given before eating, followed some hours later by a full dose of castor oil.

In **pyelitis** and **cystitis** the drug lessens bacterial pullulation in the urine. Caution should be observed, however, in administering the drug where the renal parenchyma is diseased.

Chavernac has advised the use of naphthalene by vaporization in **pertussis**. The drug may be heated in any convenient vessel, care being taken to prevent its catching fire. Rossbach commends the use of naphthalene as an expectorant in **chronic bronchitis**, given in pills, powders, or troches, and for irrigation of the nasal cavities.

Scabies is cured by the use of a 10 to 12 per cent. solution of naphthalene in olive oil or linseed oil (Fürbringer). In an ointment (5 to 10 per cent.) it is useful in **chronic eczema**, **psoriasis**, **lupus vulgaris**, etc. It has a reducing action nearly as strong as that of ichthyol and sulphur, and may be tried in all cases where these are applicable.

As a dusting powder (with $2\frac{1}{2}$ per cent. of bergamot oil to cover the odor), as a spray, or on gauze, it is useful in the treatment of **abscesses**, **ulcers**, and recent or suppurating **wounds**. Dusted into the shoe or stocking, it has been found useful in **hyperidrosis** of the feet.

In the treatment of **insect bites** rubbing the parts every few hours with 2 or 3 drops of a saturated solution of naphthalene in liquid petrolatum is recommended.

NAPHTHOLS.

The naphthols are closely related chemically to naphthalene, from which they are formed by the substitution of one hydroxyl group (OH) for one hydrogen atom, their formula being thus $C_{10}H_8O$. During the process of manufacture two naphthols are formed, the official betanaphthol being the first to crystallize and being readily separated from the alphanaphthol by boiling alcohol, in which the latter is insoluble. Betanaphthol has already been discussed (see Vol. II). **Alphanaphthol**, which is not official, is considered to be one and a half times as strong as regards its antiseptic and germicidal powers, and it is not often used internally. Its dose and therapeutic uses

are practically the same as those of naphthalene. According to Maximowitsch, alphanaphthol is superior to the beta compound for intestinal antiseptic purposes, having an antiseptic power 3 times as great and being only one-third as toxic. The latter statement, however, may be erroneous, as the toxicity of alphanaphthol is considered by many to be greater than that of the official naphthol.

SODIUM BETANAPHTHOLATE (microcidin) $[C_{10}H_7ONa]$, made by the action of sodium hydroxide on betanaphthol, occurs as a yellowish-gray or white powder, soluble in 3 parts of water. It possesses strong antiseptic properties, and may be used in 0.3 to 0.5 per cent. solution in diseases of the ear, nose, and throat, and in 3 to 5 per cent. solution as a surgical antiseptic for instruments, bandages, etc.

BETANAPHTHOL BENZOATE (benzonaphthol; benzoyl naphthol) $[C_{10}H_7.C_7H_5O_2]$, a combination of benzoic acid and betanaphthol, occurs as a whitish powder which darkens with age. It is soluble in alcohol, but not in water. It is antiseptic and diuretic in doses of 4 to 8 grains (0.26 to 0.52 Gm.). With equal doses (2 grains—0.13 Gm.) of bismuth salicylate and $\frac{1}{2}$ grain (0.032 Gm.) of Dover's powder it has been recommended by S. Solis-Cohen in cases of **infantile diarrhea**. Benzonaphthol is said to be devoid of the irritant properties of betanaphthol. Naphthol is slowly liberated from it in the intestine.

BETANAPHTHOL DI-IODIDE (iodonaphthol; di-iodobetanaphthol; naphthol-aristol) $[C_{10}H_6I_2O_2]$ is a combination of iodine and betanaphthol. It occurs as a greenish-yellow, tasteless and odorless powder, soluble in chloroform, slightly soluble in alcohol, ether, and acetic acid, and insoluble in water. It has been used chiefly as an antiseptic dusting powder on **wounds** and **ulcers**.

BETANAPHTHOL SALICYLATE (betol; naphthalol; salinaphthol) $[C_6H_4.OH.CO.O.C_{10}H_7]$, a combination of betanaphthol and salicylic acid, occurs as a white powder without odor or taste, soluble in boiling alcohol and in ether, but insoluble in water and glycerin. It is used as an internal antiseptic, antizymotic,

and antirheumatic, in doses of 4 to 8 grains (0.25 to 0.5 Gm.), in wafers, milk, or emulsion, four times daily.

NAPHTHOL-CAMPHOR (camphorated betanaphthol) is a mixture of 1 part of betanaphthol with 2 parts of camphor, and occurs as a clear, brown, syrupy liquid, soluble in alcohol. It is recommended as an application for superficial tuberculous affections, and, when mixed with oil, in the treatment of *ozena*, *coryza*, *scabies*, and *furuncles*. It dissolves the fixed and volatile oils, alkaloids in general, and iodine (Deséquelle).

W. and S.

NASAL CAVITIES AND NASOPHARYNX, DISEASES OF. See NOSE AND NASOPHARYNX, DISEASES OF.

NEPHROLITHIASIS. See KIDNEYS, DISEASES OF.

NERVES, PERIPHERAL, DISEASES OF.—The diseases to which any or all of the peripheral nerves are liable are: 1. Circulatory disorders. 2. Inflammation. 3. Degeneration. 4. Functional disorders. 5. Neoplasms.

The circulatory disorders of any importance are: (a) Ischemia. (b) Hyperemia.

(a) ISCHEMIA.

This is a frequent accompaniment of general anemic states, and is also seen as a result of obstruction of the blood-vessels of the nerves from atheroma or other cause, and also occurs with the vasomotor neuroses. The condition is chiefly of theoretical interest, since a positive diagnosis is always difficult and frequently impossible, the symptoms being various and oftentimes vague and lacking in characteristic features. Anemia is doubtless in some instances a cause of neuritic pains and neuralgias, and some of the pains and paresthesias accompanying the atheromatous

arterial changes of old age are doubtless due to this condition. Almost any of the ill-defined peripheral motor and sensory abnormalities of the nerves may at times be presumptively traced to anemia.

Total or complete, permanent or transient interference with the supply of blood to a peripheral nerve may entail serious functional disturbance and even degeneration of the nerve. Desplats and Baillet (*Arch. des mal. du cœur*, Aug., 1911).

Time has confirmed the theory that neuritis may be caused by waste products where deficient oxygenation and nutrition of a nerve prevails. Thus, the optic nerve may suffer from ischemia after severe gastric hemorrhages; severe polyneuritis may also be traced to excessive bleeding. Duhot (*Paris méd.*, Feb. 15, 1919).

Sajous, as far back as 1907, urged that the accumulation of wastes in nerves debilitated by exposure to cold, traumatism, etc., and the resulting ischemia was a prominent cause of neuralgia, neuritis, etc. The neuralgia or headache which begins early in the morning when the circulation is at its lowest ebb may sometimes be relieved merely by removing an extra pillow which by raising the head too high interferes with the gravitation of blood to the sensitive nerves. EDITORS.

TREATMENT.—The successful treatment of the condition is based upon a recognition of its primary cause, and is directed toward the removal of this cause, together with the use of general tonics and hygienic measures calculated to improve nutrition and circulatory activity, especially strychnine. In the aged and feeble, with diseased arteries, all remedial measures may fail.

(b) HYPEREMIA.

This condition likewise is only recognizable with difficulty, although the symptoms are somewhat more definite and characteristic than are

those of ischemia of the nerves. The most commonly observed symptoms are muscular weakness, tenderness or pressure along the course of the nerve; pain, darting, stabbing, or neuralgic in character, together with sensory perversions. A true neuralgia may have as its basis hyperemia of the nerves. The symptoms are, it will be seen, much the same as those of an early stage of neuritis.

ETIOLOGY.—The causes of hyperemia of the nerves are: Adjacent inflammations, mechanical injuries, exposure to cold; bacterial, alkaloidal, metallic, and other poisons; rheumatism, gout, and other diathetic diseases; in short, the causes which, when intensified or prolonged, cause neuritis.

TREATMENT.—The best results in treatment are obtained from **cold applications, leeches, cupping, and counterirritation.** **Massage and hydrotherapeutic measures** are beneficial in chronic cases. Of internal remedies, **potassium iodide** and preparations containing **iron** give the best results. **Sodium bromide** is efficient in most cases by reducing the sensibility of the sensory terminals.

NEURITIS.

Inflammation of the nerves is, in most instances, associated with more or less degenerative change in the nerve-fibrils of the affected nerves. When the morbid process involves the nerve-sheaths and connective-tissue structures in particular we have an *interstitial neuritis*, and the changes are chiefly inflammatory in nature. When the disease locates itself in the nerve-fibrils it gives rise to *parenchymatous neuritis*,—a condition partaking more of the character of a degeneration than of a true inflammation. In practice these

two morbid states are usually combined,—*diffuse neuritis*,—so that, as indicated above, the so-called “neuritis” embodies both inflammatory and degenerative changes. There are many named varieties of neuritis, based upon etiological differences, intensity of the disease, its distribution, etc., and much confusion results therefrom. The practically important varieties are the following:—

(a) Traumatic neuritis, resulting from direct mechanical injury to the nerve, as from blows, wounds, pressure, etc., or through central disturbances awakened by the traumatism, which in turn give rise to peripheral neuritis, with hysterical phenomena in some cases.

In all of the writer's cases of brachial pressure neuritis there were definite signs of pressure on the dorsal root or lower trunk of the brachial plexus of the left side. While the condition suggested a cervical rib, there were vague shoulder and other pains which masked the typical symptoms of the anomalous rib. W. Mercer (Edin. Med. Jour. Dec., 1923).

(b) Neuritis from exposure to cold, sometimes called rheumatic, on good ground, as a polyneuritis.

Rheumatic polyneuritis is a well-defined clinical entity; it may be the work of the bacilli or the result of toxemia or exposure to excessive heat or cold. The symptoms are sensory, motor, and trophic, the first named being the most pronounced and often leading to the diagnosis of neuralgia or gout. The pains commence insidiously, at first merely a sensation of tension in a limb or over several nerve areas. At first there are intervals free from discomfort or pain, but the pains gradually become more continuous and increase in severity on changes in the weather or with fatigue. The nerves are not tender except at the

emerging points of the main trunks. Schulhoff (Med. Klinik, June 15, 1913).

(c) Neuritis caused by extension of disease from adjacent parts (tuberculosis, syphilis, bone disease, etc.).

(d) Forms of neuritis resulting from the presence of bacterial poisons in the blood, exemplified in the neuritis accompanying or following typhoid fever, malaria, variola, syphilis, diphtheria, etc.

Report of 2 cases of postinfluenzal multiple neuritis. The first was in a man of 24 years. He showed loss of power in the legs and arms; absence of biceps, triceps, patellar and Achilles reflexes on both sides; flexion on plantar stimulation; pain, touch, heat and cold diminished in the distal portions of the upper and lower extremities; sense of position and sense of vibration greatly impaired in all 4 extremities; stereognostic perception lost in both hands; deep pressure markedly involved in both hands and feet; nerve trunks tender on deep pressure.

There was in this patient normal faradic response and slight diminution of galvanic excitability.

The blood, spinal fluid, urine and gastric contents, upon examination, were found normal.

The second case was similar. The prominent ataxia and loss of deep sensibility in these 2 cases were unusual findings, and the posterior columns of the cord may have been involved in addition to the peripheral nerves. G. Wilson (Jour. Amer. Med. Assoc., May 19, 1923).

(e) Neuritis resulting from the action of poisons introduced from without, such as alcohol, lead, arsenic, mercurials, opium, etc.

The liver derangement has much to do with the development of the polyneuritis; some toxic product normally taken care of by the liver is allowed to remain unmodified or is modified in some abnormal man-

ner, and it acts on the nerves, inducing the polyneuritis. The suggestion is tentatively advanced that the recent research on the peculiar sensitizing properties of fluorescent substances (Tappeiner and Hausmann) may explain the polyneuritis in these cases as the result of the action of urobilin in the blood, urobilin being a fluorescent substance. Hematoporphyrin might also be considered from this standpoint. In the lead poisoning case the polyneuritis was of the Landry type and the patient presented intense urobilinuria and urobilinemia. Eppinger and Arnstein (Zeit f. klin. Med., Bd. lxxiv, Nu. 3-4, 1912).

(f) The endemic or epidemic form of neuritis, seen in tropical islands and seacoast countries, the well-known "beriberi" (see BERIBERI, Volume II).

(g) The neuritis accompanying certain skin eruptions or other trophic changes (see HERPES ZOSTER, Volume V).

Whatever the pathological nature or etiological origin of neuritis, if a single nerve or small group of adjacent nerve-trunks be affected it is called a *simple neuritis*. If a number of nerves in different portions of the body be simultaneously invaded there exists a *multiple neuritis*. The neuritis from mechanical injury, exposure to cold, and other local causes is usually simple; the general infections, drug poisonings, and other toxemias give rise most often to multiple neuritis. Of course, there are exceptions to these rules, since a general toxemia may produce only localized effects—a simple neuritis—and a mechanical injury may involve a large nerve-trunk or several large nerves and give the symptoms of a multiple neuritis, as has been seen in cases of pressure upon lumbar and sacral nerves of

a large aneurism. A simple neuritis is usually *interstitial*; a multiple neuritis is apt to be chiefly *parenchymatous*.

SIMPLE NEURITIS.—A simple or localized neuritis arises from exposure to cold, involving in such cases nerve-trunks which lie near the surface of the body, the most frequently observed clinical form being *Bell's paralysis*, or *facial paralysis*; from traumatism,—blows or wounds, and from pressure, as by morbid growths, aneurisms, sleeping upon the arms, or crutches used long or injudiciously (*crutch paralysis*).

The 2 commonest types of neuritis (facial and musculospiral) are instances of motor neuritis and hence unassociated with pain. A posterior root neuritis is generally unattended with tenderness at the site to which the pain is referred. In root disease of any severity "anesthesia dolorosa" is present. Pain in an extremity is rarely due to neuritis, the commonest causes being root involvement, arthritis and diseased blood vessels. G. Wilson (Jour. Amer. Med. Assoc., May 19, 1923).

Simple neuritis may also arise from tuberculous or other disease which involves the nerves by extension from adjacent affected parts.

There are to be found in the literature 136 instances in which the femoral nerve has been the seat of an inflammatory process originating from some internal disorder. The disease has been observed 84 times as a post-partum complication, once as a congenital affection; 8 times as a primary condition, and 3 instances have been referred to which the writer has been unable to verify. The remaining 40 cases are distributed among 15 different disorders. In a few instances the inflammation has extended to adjacent nerves, but in each case the most pronounced symptoms have been confined to the femoral distribution. The onset of

the disease may be acute or subacute. The commonest and earliest symptom is pain in the distribution of the crural nerve or one of its neighboring branches. In the course of a week, or even a month, if the onset be subacute, the pain becomes more persistent, of wider distribution, greater intensity, and of a continuous paroxysmal nature with nocturnal exacerbations. The character, location, and extent of the pain are quite distinctive. Except in the mildest cases, there is always some motor disturbance. Weakness and "giving way" of the knee are common complaints, and there is some difficulty in raising the leg from the bed when the knee is fixed. There is usually moderate wasting of the muscles on the front of the thigh. The superficial reflexes, epigastric and abdominal, may or may not be altered. Slight electrical changes are usually to be found in the muscles of the affected side. Byrnes (Jour. of Nerv. and Mental Dis., Jan., 1914).

Symptoms.—The symptoms of simple neuritis vary with the cause, nature, and location of the disease, but the true neural symptoms are essentially the same in all, consisting in perversion, exaltation, or, it may be, entire abolition of function of the nerves involved. There is usually pain, of a stabbing, darting character, felt in the parts to which the nerve is distributed, with some pain and tenderness along the course of the nerve. This pain is partly due to pressure or irritation of the *nervi nervorum*, and may be very intense and distressing or may, as is often the case in mild forms of neuritis, cause little or no inconvenience. There is occasionally edematous swelling and redness of the skin over the point of greatest inflammatory activity, and trophic cutaneous affections, sweating, and swelling of, and effusions

into, joints sometimes appear. Tactile sensation is impaired in the affected area, and numbness and formication are frequent. Weakness in the muscles supplied by the affected nerves is the rule, reaching in the severer cases a complete paralysis. Muscular twitchings and spasmodic contractions are sometimes noted. In the severe and long-continued cases there is apt to be great atrophy of the affected muscles, which may be followed by contractures of fingers or toes or other parts involved. The nutrition of the hair and nails is often defective, leading to falling out or grayness of hair, deformities or dropping away of nails, etc.

Case in which a prophylactic injection of 10 c.c. (2½ fluidrams) of antitetanic serum, following a similar injection given four years before, caused an immediate local urticarial and inflammatory reaction, and later (nine days after the injection) alternating attacks of general urticaria and cardiac weakness, lasting for two days, and accompanied by vomiting, diarrhea, oliguria, albuminuria, and rapid loss of strength. Although the condition seemed critical, quick recovery followed. Two weeks later there developed on the side of the injection paralysis of the serratus magnus and other muscles, with rapid wasting. The phenomena of serum intoxication and anaphylactic shock seemed to coexist. Thaon (*Revue de méd.*, Sept., 1912).

The electrical reactions in simple neuritis vary with the intensity of the disease, being in the milder cases nearly or quite normal, but showing in all of the severe forms a partial or complete reaction of degeneration.

The duration of a simple neuritis depends chiefly upon the severity or curability of the initial lesion. The symptoms may pass off in a few days,

or may persist for months. Recovery is the rule, and is always obtained, provided the cause is one which can be removed. In very unfavorable cases some permanent contracture or paralysis may result.

Pathology.—In simple neuritis the changes are chiefly localized in a limited portion of the nerve-trunk, only the degenerative changes in nerve-fibers, where such a parenchymatous lesion is present, extending along the entire distal portion of the nerve. At the point of injury the nerve-trunk is red, swelled, and infiltrated with lymphoid elements, and may be surrounded by a gelatinous exudate. The changes involve especially the perineural and interstitial connective-tissue framework. In mild cases the nerve-fibrils themselves are slightly, if at all, involved; in severer cases, or where the fibrils have undergone compression from swelling of connective-tissue structures, the nerve-fibrils show the alterations of parenchymatous neuritis; their myelinic sheaths are fragmented, the nuclei of the sheath of Schwann and of the internodal cells are increased in number, or may seem swelled; in still more severe cases the axis-cylinders show marked degenerative alterations, become varicose, swell, disintegrate, and even entirely disappear, the appearances being then nearly identical with those of a true Wallerian degeneration. These changes in the axis-cylinders necessarily involve all of the nerve-fibers lying below the seat of injury, but are usually arrested at the first node of Ranvier above, although in some cases they may extend upward, even quite to the cord. The blood-vessels at the seat of an injury are

often distended, and minute hemorrhages into the nerve are of not infrequent occurrence. The disease may go on to complete destruction of the nerve-elements, the degenerated fibers being replaced by connective tissue and by fat-cells: a condition, when the fat-deposits are abundant, called by Leyden "lipomatous neuritis." Regeneration begins after a short time, and, if the original nerve injury be removed, the nerve may, even in very severe cases, ultimately regain its former healthy state.

Treatment.—As a necessary preliminary to any treatment, the cause of the disease must be removed. After this, **rest** of the affected part, absolute and continued for several days, should be insisted upon. The application of **splints** to limbs is sometimes advisable. **Heat**, especially **moist heat**,—as from steam, poultices, or fomentations,—gives great relief from the pain. **Counter-irritation** by **mustard plasters** or other means is sometimes equally efficacious. In many instances the **galvanic current** used in strength sufficient to redden the skin gives immediate and wonderful relief. Occasionally in early stages **ice** locally applied will give more relief than anything else. Of internal remedies, **phenyl salicylate**, **aspirin**, the **salicylates**, and the whole series of coal-tar derivatives—in particular, **antipyrin**, **acetphenetidin**, and **acetanilide**—may be used in the confident expectation of obtaining measurable relief from the pain.

Series of 32 cases treated with **nitroglycerin** after the method suggested by Krauss, of Buffalo. Beginning with $\frac{1}{100}$ grain (0.0006 Gm.) every eight hours the interval was reduced one hour in every twenty-

four until the full physiological action of the drug was manifest, or the patient was taking $\frac{1}{100}$ grain (0.0006 Gm.) every three hours, at which interval it was continued. **Sodium bromide** controls the flushing and headache. In acute cases the effect was marked within forty-eight hours. In chronic cases **ammonium** and **potassium iodide** in progressively increasing doses hastened the action of the nitroglycerin. The **actual cautery** was also used over the nerve. Stevenson (Med. Rec., May 16, 1908).

For pain, especially that associated with rheumatic or gouty cases, the following mixture is recommended:—

R *Antipyrin* gr. v-x (0.3-0.6 Gm.).

Sodium salicylate . gr. x (0.6 Gm.).

Caffeine citrate.... gr. v (0.3 Gm.).

Aromatic spirit of ammonia f3ss (2 c.c.).

Chloroform water,
q. s. ad..... f3ss (15 c.c.).

For the arteriosclerotic cases a mixture containing **nux vomica** and **potassium iodide** is often very effective. **Acetylsalicylic acid**, gr. xv (1 Gm.), is often very useful in the milder cases. Howell (Pract., Mar., 1914).

When other remedies fail the local hypodermic use of **morphine** is, where pain is very intense, justifiable. The early use of mercurials—**calomel** or **blue mass**—is often attended by good results. In any case the bowels should be kept open by **salines** or a simple **purgative pill**. Attention should be paid to the general health. In most instances **tonics** and **alteratives** will be found beneficial.

The benefit from deep injections of **alcohol** in neuritis and neuralgia is extolled as a substitute for removal of the Gasserian ganglion, as the toxic degeneration that follows the injection answers practically the same purpose as gasserectomy. The writer's experience confirms the possibility of subsequent toxic degenera-

tion of the nerve; on this account the method should not be applied to motor or mixed nerves except as a last resort. He treated 12 patients with severe sciatica by local injection of alcohol, and 8 were either entirely or nearly cured, but 1 patient developed complete paralysis of the peroneus nerve, which persisted complete for nine months and then gradually subsided in the course of the next three months. Erb had a similar experience in 3 cases in his private practice. With all its advantages, therefore, the method has its drawbacks. Fischler (Münch. med. Woch., Aug. 6, 1907).

Hot-air applications accomplish two equally important objects: they alleviate the pains, which are the principal symptom of the disease, and at the same time they cure the disease itself. The cure is effected most likely by the production of an active hyperemia, not only in the skin to which the heat is applied, but also in the underlying tissues, including the affected nerve-trunks. After an application the skin is very much reddened, and at the end of a week the area is browned as from sunburn. The process of repair is stimulated and the course of the disease considerably shortened. In the milder forms of the disease, which are fully as common as the severer forms, the hot-air treatment is as near an approach to a specific as we could wish for. Stieghtz (Med. Record, July 8, 1911).

The writer places long **electrodes** consisting of absorbent cotton wrapped in gauze parallel in pairs along the limbs or spinal column. The current is transmitted through metallic bands of suitable length, intensity of current being 60 to 80 milliamperes for an arm and 100 to 125 for a lower limb. The sitting should last three-quarters to one hour, and be frequently repeated. The method was used in nearly 600 cases, with excellent results. Traumatic myelitis was benefited. Hirtz (Semaine méd., May 28, 1913).

The writer found **cataphoresis** of the very greatest use in relieving pain and shortening the attack in cases of rheumatic or gouty origin. The drugs introduced are either 2 per cent. **sodium salicylate** or **iodine**. For the former the cathode is used, for the latter the anode. It is preferable to have the arm treated by **hot air** or **hot compresses** before ionization is begun; the object of this is to get the skin thoroughly moist, thus enabling large currents to be used painlessly, whereby the entrance of the iodine or salicylic acid ions is facilitated. The **limbs** should be **kept warm** by being wrapped in wool and the weight of the **arm supported by a sling**. Howell (Pract., Mar., 1914).

Sodium iodide administered intravenously with very satisfactory results. The author has been able thus to get a larger amount of iodide into the patient with less gastric or other disturbance than by any other method. From 30 to 120 Gm. (1 to 4 ounces) were given at a time without deleterious effect. L. Stark (Nebr. State Med. Jour., Jan., 1924).

Treatment by **electrolysis** gives good promise of relief in cases in which the lesion is of the interstitial type, being the result of inflammation of the nerve sheath. W. B. Jones (Brit. Med. Jour., Jan. 17, 1925).

Operative treatment advised in all cases of traumatic neuritis of the ulnar nerve in the postcondylar groove. The procedure is simple and effective, and consists of anterior displacement of the nerve-trunk. H. Platt (Brit. Jour. of Surg., Jan., 1926).

After subsidence of the acute stage and after all tenderness, redness in skin, pain in parts, etc., have disappeared, systematic **massage** and the use of **faradic stimulation** to the muscles will hasten restoration of function in muscles and cutaneous surface. The presence of varicose veins in the affected limb calls for support, e.g., an **elastic stocking**.

A simple and most satisfactory treatment is to map out the tender spots along the affected nerve. A pledget of cotton firmly compressed into a ball the size of a knuckle is then saturated with **fuming hydrochloric acid**. A strip $1\frac{1}{2}$ inches wide is then painted with the acid along the painful area. The slight smarting produced passes off in a few minutes and the skin is not harmed. This is repeated twice a week until pain and tenderness cease. Saintsbury (Lancet, June 16, 1917).

MULTIPLE NEURITIS, OR POLYNEURITIS.

DEFINITION.—This disease (also termed disseminated neuritis and peripheral neuritis) is a parenchymatous neuritis affecting many peripheral nerves at or about the same time.

VARIETIES.—Numerous varieties and forms of multiple neuritis are recognized, and of these the more important have received distinguishing names, as mentioned below. The varieties, as in the case of simple neuritis, arise from differences in nature, causation, severity, and location of the morbid process. The causes of multiple neuritis are: bacterial infection, toxic substances in the blood, anemia, and dyscrasic states; in short, any state of toxemia or malnutrition.

SYMPTOMS AND DIAGNOSIS.

—The disease may come on suddenly and reach its greatest intensity within a few days (acute bacterial infections), or may show a slow and insidious onset (alcoholic and cachectic forms). The characteristic and ever-present features of the clinical picture are the abnormalities of nerve-reaction: *i.e.*, alterations in sensory, motor, reflex, and trophic function of the nerves involved.

The writer has observed at the front and in civil life an acute, severe form of widespread polyneuritis. The onset is generally rapid with malaise or fever and no local manifestations. The pains develop in the legs and lower part of the back, usually on the second or third day, and persist. Weakness begins in the legs usually a day or so later. The paresis increases rapidly and the upper extremities affected. At about the same time the patients complain that their faces are drawn and stiff and there may also be some interference with power of articulation or swallowing. In the established disease symptoms are characteristic. The lower extremities are equally affected, flabby, without tone, and extensively paralyzed. The paralysis is seldom complete in all groups of muscles and all are often more or less uniformly affected. The feet are dropped; there may be no movement possible at the toe and ankle joints, but there is nearly always some at both hip and knee. The arms are similarly but less severely affected. The muscles of the trunk are less seriously involved than the arms, though there may be some paresis of the respiratory movements. The deep reflexes are absent. The picture closely resembles a generalized peripheral neuritis of the motor nerves. There is relatively little sensory affection, though some pain may be complained of. The sphincters are usually more or less disturbed. Vasomotor, sensory, and trophic disturbances do not occur. The course of the affection is rapid and restoration of function is usually steady and rapid. Gordon Holmes (Brit. Med. Jour., July 14, 1917).

The extraneural symptoms vary with the cause and nature of the initial morbid impulse. In the typical acute "idiopathic" cases and in cases accompanying acute infectious diseases the attack comes on with fever and the other usual features of the onset of an acute infectious malady.

A chill may be the first indication. Headache and aching in the back and limbs are frequent, as are also loss of appetite, furred tongue, constipation, and other evidences of gastrointestinal disturbance. The real nature of the case may be obscure for the first few days, but within this time the true neuritic symptoms make their appearance, and all doubt is quickly removed.

Pain along the course of the nerves in legs or arms, or both, is noted, with tenderness in the muscles as well as in the nerve-trunk. Perversions of sensation now appear, in the form of tingling, formication, diminution in tactile sense, or hyperesthesia or in rare cases anesthesia. In addition to the above-mentioned tenderness on pressure the muscles in the parts affected become relaxed and flabby; there is weakness or even in severe cases complete paralysis. This muscular weakness begins most frequently in the legs, extending upward by degrees, reaching the arms; usually these become affected some time after the symptoms in the legs are well established. In many cases typical *wrist-drop* and *foot-drop* are shown.

The paralysis may reach the muscles of phonation, deglutition, and respiration, resulting in some degree of impairment of these functions. In severe cases, especially in those of rapid onset, the pneumogastric nerve may be involved, resulting in marked tachycardia. Trophic disorders are also of frequent occurrence, such as edema, glossy skin, and herpetic eruptions in the area affected. The tendon-reflexes are usually diminished or abolished. In all save the milder cases there are changes in the

electrical reactions similar to those of simple neuritis. The muscles lose their faradic excitability and with the galvanic current show a slow, worm-like contraction, with anodal closure contraction greater than the reaction to cathodal closure.

The intensity, rapidity of onset, course, and duration of multiple neuritis vary considerably in different cases. In some the pain is scarcely noticeable, the motor symptoms predominating. In mild cases there may be only slight stiffness or weakness of the muscles, passing off in a few days. In other cases the pains are violent and excruciating, and the paralysis of the muscles is total and long continued, months elapsing before the patient regains use of the paralyzed limbs. Deaths are not infrequent, occurring during the acute stage from failure of respiration or heart-action, and in the chronic stage from exhaustion or intercurrent complications, as pneumonia, pleurisy, or tuberculosis.

In cases of multiple neuritis from other causes than acute bacterial infection there are few constitutional symptoms, a more gradual onset, and a greater chronicity. The diagnosis, also, is easier, since the neural abnormalities are not masked to such an extent by the symptoms of acute disease.

It should be remembered that the characteristic symptoms of multiple neuritis and those upon which a diagnosis must rest are the motor, sensory, reflex, and trophic nerve disorders; the gastrointestinal, cardiac, respiratory, and other occasional features may or may not be present, and to the symptoms of any multiple neuritis may be added the complicat-

ing clinical picture of some acute disease to which the neuritis is possibly due. If the nerve reactions are tested for, there will be little danger of error in diagnosis. In the acute cases of sudden onset in which tachycardia and respiratory distress, with general edema, pallor of surface, loud heart-murmurs, etc., are present the peripheral nerve disorders are masked, and the case is liable to be regarded as one of acute "heart-failure" or "Bright's disease" unless careful tests are made for neural symptoms. Chronic cases resemble in many particulars tabes dorsalis; the characteristic gait, the lightning pains, girdle sensation, and absence of muscular weakness in tabes ought, however, to render a diagnosis easy.

The condition designated *progressive neural (neuritic) muscular atrophy* is recognized by many as a form of atrophy dependent primarily upon disease of the peripheral nerve-fibers, although changes in the cord may be associated. The condition, also known as the peroneal or Charcot-Marie-Tooth type of progressive muscular atrophy, is usually hereditary, nearly always sets in between the ages of 10 and 20 years, and affects males much oftener than females. It differs from multiple neuritis in the absence of nerve tenderness.

The onset and course of acute anterior poliomyelitis are not unlike those of acute peripheral neuritis. The fact that the former occurs in children, the latter in adults, and the absence in poliomyelitis of the marked sensory symptoms of neuritis are sufficient distinguishing points in the vast majority of cases.

The disease is of frequent occurrence, coming often within the notice of both the neurologist and general practitioner of medicine. The alcoholic, syphilitic, postfebrile, and toxic forms are common in all climates. In

the southern United States malarial and idiopathic forms are often seen.

PATHOLOGY.—One has to deal in multiple neuritis with a general toxemia or nutrition deficiency in the blood, causing degenerative changes in the nerve-fibers of the peripheral nerves, associated in some instances with such inflammatory changes as were described under simple neuritis. The peripheral ends of the nerve-threads, being farthest removed from the trophic center (the cell-body), show the first and most pronounced changes. In severe cases the entire cell may become involved or be destroyed. The anatomicopathological changes are similar to those described under simple neuritis.

TREATMENT.—The treatment of multiple neuritis should first be directed toward the removal of the cause and the relief of the pain and acute symptoms; after this, measures which hasten regeneration of nerve- and muscle- fibers are indicated. In idiopathic cases a full dose of **calomel**, followed by a **saline**, is beneficial. **Intestinal antiseptics** also aid. The pains are controlled by **hot applications**, dry or moist, and by **aspirin**, the **coal-tar derivatives**, and **opium**. After subsidence of the acute stage, **massage** and rubbings of affected parts, with **faradic electricity**, give the best results in hastening regeneration. Systematic **exercise** should be advised as soon as the condition of the muscles permits of it. Tonic doses of **strychnine** and **arsenic** seem to hasten recovery. In the distressing cases in which tachycardia is a prominent symptom all heart stimulants are apt to prove of no avail, the best results being obtained from **cold applications to the chest**. In the

paralytic cases where, after long-continued helplessness, contractures and permanent deformities are threatened, **passive movements** and, if need be, **fixation of limbs** by means of properly adapted **splints** may be required.

The more important varieties of multiple neuritis are the following:—

Syphilitic Neuritis.—In this variety the onset is afebrile and insidious, acute, active symptoms being wanting. The course is chronic. Some cases resemble *tabes (syphilitic pseudotabes)*.

Syphilitic polyneuritis is an uncommon condition. Of the author's 2 cases, 1 was seen late in the secondary stage and the other in the tertiary stage. Koehler (Deut. Med. Woch., Aug. 14, 1925).

The treatment comprises the use of **arsphenamin, mercury, iodides, hot baths, massage, and electricity.**

Alcoholic Neuritis.—Caused by chronic alcohol poisoning. Gradual onset, without fever or disturbance of general bodily functions. Chronic course. Cure usual, through **removal of the cause.**

Arsenical neuritis, saturnine neuritis, and other related forms are due to injudicious or excessive use of arsenic, lead, or other drug. Emetine has caused a number of cases.

These are readily curable through **removal of the cause.**

Postfebrile neuritis, following typhoid or other fever, **diphtheritic neuritis, scarlatinal neuritis,** etc., are caused by the poisons of these infectious diseases. The neural symptoms are complicated by the features of the associated germ disease. Disappearance of the acute disease is followed by recovery.

Case of polyneuritis following diphtheritic infection of a cholecystectomy wound. Paresis of accommodation and

of the uvula developed 3 weeks later. Reinhold (Deut. med. Woch., Dec. 11, 1925).

Malarial neuritis occurs in malarial localities, not always accompanying or following malaria, but occurring in some persons in a community while others suffer from malaria. The onset, course, clinical picture, and terminations are similar to those of the idiopathic forms. It resembles beriberi in some particulars.

Case of malarial neuritis in a young man. The deltoid became paralyzed suddenly and had remained so for 4 months. Out of 37 cases of malarial neuritis in the literature only 9 attended the pernicious type of malaria. Paiseau, Schaeffer and Alcheck (Bull. Soc. méd. des hôp. de Paris, Nov. 18, 1921).

Neuromyositis.—Senator in 1888 first used this term to distinguish cases presenting symptoms of both neuritis and myositis. Only a few instances have been recorded, the majority in alcoholics. The nervous symptoms are those of a multiple neuritis, and seem to have been more prominent than the muscular symptoms, which vary from tenderness to swelling and pain on movement. Characteristic features are tenderness over the nerve-trunk, sensory losses, loss of reflexes, ataxia, and muscular atrophy.

Tuberculous neuritis, rheumatic neuritis, septicemic neuritis, diabetic neuritis, and many other forms are spoken of by writers.

Multiple neuritis may be divided into the toxic exogenous, toxic endogenous, infectious, and cachectic forms. Carbon monoxide and bisulphide occasionally cause it. Asymmetric neuritis is a feature of typhoid and paratyphoid, and has been known to occur after acute tonsillitis followed by nephritis.

The diabetic neurotoxin is probably of the autotoxemic deficiency type. Septicemia is a not uncommon cause, sometimes following a very insignificant wound. Tuberculosis and malignant disease are rare sources. In the autotoxemic group, the neuritis of beriberi is comparable to that of diabetes. Some puerperal cases are autotoxemic. Hematoporphyrinuric neuritis is unusual, with high pulse rate but no fever, and may be familial. Poliomyelitis and polyneuritis may be the same process affecting different parts of the same neuron. W. Harris (*Lancet*, Oct. 21, 1922).

Six cases of tuberculous neuritis, sensory in type, were observed among 850 tuberculous patients; 5 of these were in women. Only 1 instance of both sensory and motor polyneuritis was noted among 2000 cases. Lévy-Valensi (*Médecine*, Feb., 1925).

Pregnancy and parturition neuritis is also a recognized form.

Job has recorded 16 cases of myelitis or polyneuritis occurring in the course of toxic vomiting in pregnant women. The pulse rate had always been over 100 before the signs of paralysis developed, confirming the necessity for active measures whenever the pulse exceeds 100 in the vomiting of pregnancy. Five women died; 6 were delivered at term, but most were left with severe functional disturbances. In 5 cases the gravity of the symptoms led to early interruption of the pregnancy and the outcome in these was by far the most favorable.

Endemic neuritis, or beriberi, is seldom seen save in the tropics, near the seacoast. (See **BERIBERI** in Volume II.)

Enterogenous Multiple Neuritis.—Autointoxication of intestinal origin is undoubtedly a prominent factor in many cases.

According to Von Noorden enterogenous multiple neuritis may be excited even in the presence of diarrhea, the latter being merely a reflex from the irritation of the feces. It may assume the form of mucous colitis. The proctoscope in such cases shows the

real nature of the condition. Owing to the absorption of some neurotropic substance, neuralgiform pains appear here and there, and in some instances the affected nerves are sensitive to pressure. Similar pains may seem to affect muscles and joints, and are always fugacious.

Peculiar case of recurrent hypertrophic neuritis in a male of 18 years, featured by prolonged attacks of extensive flaccid paralysis, with loss of reflexes, pain, and electrical changes, followed by complete functional recovery. Previous similar attacks had occurred at the ages of 4 and 17. The health was otherwise good. The nerve trunks were hypertrophied and hardened. Nattras (*Jour. of Neurol. and Psychop.*, Aug., 1921).

Case of multiple neuritis following a preventive injection of 10 c.c. of anti-tetanic serum. There was no history of any serum injection earlier in the patient's life. R. Marchal (*Arch. méd. belges*, May, 1923).

An artificial pneumothorax was followed by both motor and sensory neuritis in the 4 limbs. Lévy-Valensi (*Bull. Soc. méd. des hôp. de Paris*, Dec. 9, 1924).

Report of an obscure, pseudotabetic type of polyneuritis observed in 2 girls aged 6 and 11 years. In the older child there was some fever and a history of a fright just previous to the onset of ataxia. The younger child had no acute symptoms. The condition developed insidiously and progressed until the patients were unable to walk or feed themselves. Pain and tenderness were absent. Complete recovery took place within 2 months. Navarro (*Semana méd.*, Oct. 29, 1925).

Aside from removal of the cause, the treatment of multiple neuritis calls for **rest in bed** as an all-important adjunct. **Pressure of the bed-clothes upon the affected areas should be avoided.** **Nutritious food** is indicated where asthenia exists, but the possibility of enterogenous autointoxication as a cause should be re-

membered. When the urine shows an abnormal amount of acid, **alkalies** are effective.

In autointoxication neuritis some cases respond most rapidly to a pure **milk diet** or modifications of milk, such as **sour milk**, **yoghurt**, **kefir**, etc. In other instances, **farinaceous food** or a **mixed vegetable diet** gives better results. In some cases it was found to be of decided benefit to have the patient take nothing for some days but a solution of **sugar**. There are cases in which an **animal diet** deserves the preference, to be given a short time only. Von Noorden (Jour. Amer. Med. Assoc., Jan. 11, 1913).

The writer recommends **hot saline solution** injections into the painful area, the amount injected varying with the location of the painful nerve. For the sciatic he injects 200 c.c. (6¼ ounces), for the anterior crural 50 c.c. (1½ ounces), etc. The needle is inserted first and if no blood appears, the syringe is attached after all air in it besides the fluid is carefully expelled. The pain fails to recur in months (2 years in one instance); when it does, the injection will again promptly relieve. Alfred Gordon (Therap. Gaz., June 15, 1916).

For pain, **belladonna** and **morphine** may be used jointly, but guardedly—hypodermically or directly into the most painful area. **Scopolamine hydrobromide** is also useful. The local application of **adrenalin ointment** or **veratrine ointment** or, again, **hot lead water** and **laudanum** may prove useful. **Cocaine anesthesia** induced as for surgical operations is sometimes necessary where the pain is extremely acute. The general measures indicated in simple neuritis may also be applicable, but the **salicylates** and **antipyrin**, etc., are not always efficient. This applies also to **mercurials** and the **iodides** unless the case be distinctly of syphilitic origin.

A formula successfully used by Willige in 5 cases was as follows: **Sodium cacodylate**, 1.5 Gm. (23 grains); **cocaine hydrochloride**, 0.1 Gm. (1½ grains); **liquid phenol**, 3 drops; distilled water, to make 50 c.c. (1¾ fluid-ounces). The treatment began with 0.4 c.c. (6 minims), increased by 0.1 c.c. (1½ minims) daily until 2 c.c. (32 minims) were reached; this amount was continued for two weeks, then reduced gradually to 0.4 c.c.

In chronic multiple neuritis following influenza, affecting in particular the supraorbital nerve, the writer recommends **intravenous injection of salicylates**. He used a solution of **sodium salicylate**, 0.43 Gm. (7 grains); **caffeine**, 0.05 Gm. (¾ grain), and water, to 3 Gm. (48 minims). Rubens (Deut. med. Woch., June 2, 1921).

Case in a male of 19 following about 10 weeks after an acute throat condition, probably diphtheria, in which **adrenalin chloride**, 0.5 mgm. (½₃₀ grain) was given and increased daily to the limit of tolerance. After a month the patient was able to walk, and complete recovery followed. De Valle y Aldabalde (Siglo méd., Feb. 11, 1922).

Body irradiation with the air-cooled **quartz mercury lamp** advocated. The **static wave current** is then applied as in sciatic neuritis, the patient being forewarned that the soreness may be aggravated for a few days. If neurotic hyperesthesia manifests itself, static treatments are replaced for 1 or 2 days by the **high frequency current**. This neuritic therapy is usually combined with a 15-minute treatment of wave current applied by the spinal electrode to the lower dorsal and lumbar spine, using a long slow spark. Persons with poor peripheral circulation respond to **resonator sparks** rapidly applied over the whole leg and foot surface. The later stage of the treatment, i.e., after the neuritic soreness and pain have been relieved, consists in the use of the **galvanic sinusoidal current** for 20 minutes at a time if the patient can tolerate it, the dorsal pad being retained by his weight in the recumbent position, and the small pad applied to

the foot, usually the sole. When the patient can stand on his feet again, overexertion must be strictly avoided. W. Martin (Amer. Jour. of Electr. and Radiol., Dec., 1923).

Dry heat, wrapping the painful areas in **cotton-wool pads**, and **warm baths** as hot as can be readily borne have all given good results.

An important feature is to prevent dropping of the feet; these should be supported by **splints** or by **sand-bags**. **Postures** assumed for the relief of pain **should be gently changed** so as to avoid adhesions within the joints and invalidity.

In the polyneuritis due to alcohol, which affects mainly the extremities, the **use of alcohol should cease** at once and **sodium bromide** given to subdue the hyperesthesia of the sensory terminals.

FUNCTIONAL DISORDERS OF NERVES.

VARIETIES.—The functional disorders of the peripheral nerves may be classed as the motor, sensory, and mixed forms.

The **motor** functional neuroses of peripheral origin are:—

(a) **Recumbent palsy, night palsy, or waking numbness**, characterized by temporary paralysis of one or more extremities, is noticed after lying still for a time or upon awakening in the morning. The symptoms are much the same as those seen when a nerve is compressed, as when a limb “goes to sleep”; but are not caused by pressure, and should not be confounded with the pressure paralyses. It is a rare condition, occurs in neurotic subjects, and its causation and pathology are unknown.

(b) **Spasm and tremor**, occurring from overuse of muscles and fre-

quently associated with some form of **occupation neurosis**.

The peripheral **sensory** neuroses are:—

(a) **Neuralgia**, elsewhere described.

(b) **Paresthetic neurosis**, an affection closely akin to and sometimes associated with the waking numbness above mentioned. It is a condition of little practical importance.

NEOPLASMS OF NERVES.

Tumors growing in or upon the nerve-trunks are either *true neuromata*—i.e., tumors composed of medullated nerve-fibers or other nerve-tissue—or are *false neuromata*,—i.e., composed of other than nerve-tissue. The “false” neuromata are usually of secondary origin, i.e., extend to the nerve from adjacent structures, the most common kinds being fibroma, sarcoma, myxoma, and the syphilitic and tuberculous growths. They need not be considered here, attention being directed only to the true nerve tumors.

NEUROMA occurs singly or in numbers reaching into the thousands. When multiple, neuromata are usually small, and form shot-like, but quite painful nodules under the skin. When few in number they are apt to be larger in size, being occasionally an inch or more in diameter. The causes of neuroma are, in the multiple form, hereditary predisposition, and, in the simple form, injuries to the nerve-trunk from blows, surgical operations, etc. The knob-like masses which develop upon the ends of the nerves of the stump after amputation offer a good example of this form of neuroma.

Symptoms.—The symptoms of neuroma, beyond the presence of the tumor, are often *nil*. In some in-

stances, however, there is pain, paresthesia, or paralysis in the affected nerve area. Occasionally the pain is intense, distressing, and neuralgic in character, as is seen in *postamputation neuromata*.

Treatment.—No treatment is called for unless there is pain or other interference with nerve function, when surgical measures, usually a total **excision**, are called for and give relief.

When examined microscopically true neuromata are found to consist of nerve-fibers, medullated or non-medullated, with occasionally a few ganglion-cells interspersed, these nerve-elements being mixed with some fibrous tissue. When the fibrous tissue is abundant the growth is spoken of as *fibroneuroma*.

DISEASES OF SPECIAL NERVES.

The several conditions of general disease already described may, when involving special nerves, give rise to well-defined clinical symptom-groups meriting brief description.

Diseases of the nerves of *special sense*—the olfactory, optic, auditory, etc.—are dealt with by specialists and are, to a large extent, devoid of general interest. The affections of the optic nerve, of which neuritis is the most important, are of value in the diagnosis of intracranial lesions.

Disease of the third, fourth, and sixth pairs of cranial nerves leads to abnormalities of ocular movement, whose consideration falls within the domain of the eye specialist, although the lesions are often of value in diagnosis of brain diseases.

The most important disorders of the fifth cranial nerve are neuralgia and headache, elsewhere considered.

The seventh cranial nerve may be affected by spasm or convulsive tics, or by the not uncommon and clinically important "Bell's palsy," or facial paralysis.

FACIAL PARALYSIS.

This is a motor paralysis affecting usually the muscles of one side of the face.

SYMPTOMS.—The onset of a facial paralysis is usually sudden, or of rapid development, and is indicated by loss of power in the muscles of one lateral half of the face, with loss of emotional as well as of voluntary movements. The affected side is expressionless and smooth, the lower eyelid droops, and the eye cannot be entirely closed. The tears accumulate and run down the face. The lips are relaxed and powerless, and ability to drink, chew, articulate, etc., is impaired. The mouth is drawn toward the affected side, this and other evidences of paralysis being exaggerated when the patient laughs or smiles. The affected side may show some congestion or circulatory defect, and occasionally an herpetic eruption appears. The soft palate and tongue are not involved, although, on account of the displacement of the mouth, the tongue seems to deviate from the median line. The sense of taste in the anterior part of the tongue is lost in a small proportion of cases. There are few or no sensory abnormalities.

The electrical reactions are the same as are seen in other forms of peripheral neuritis, their exact character depending upon the severity of the case, and for this reason possessing an especial value in prognosis. Thus, if the electrical reactions are nearly normal the case is a mild one,

and recovery will most likely take place within a few weeks. If the excitability of the nerve to galvanic and faradic currents is lessened and that of the muscles to galvanic current increased and formula altered (An.Cl.C.>K.Cl.C.: contraction sluggish) the case is still favorable, recovery being probable within six to eight weeks. When complete re-action of degeneration is present,—that is, when faradic and galvanic excitability of nerve is lost, faradic excitability of muscle lost, galvanic excitability of muscle increased, and formula and nature of contraction altered as above,—the case is serious and will not recover for many months.

The usual outcome of a peripheral facial paralysis is complete recovery. In the few cases which terminate unfavorably the paralysis and resulting facial asymmetry may be permanent. There is atrophy of facial muscles in all severe cases, and some degree of atrophy as well as some contracture may, in the more serious cases, persist.

DIAGNOSIS.—The diagnosis of a facial palsy is simple, inspection being all that is required in the majority of cases. The only question is whether the lesion is central or peripheral. The peripheral cases show changes in electrical reactions, impairment of emotional movements, loss of reflex movements, and persistent paralysis of eyelid, these conditions being reversed in central paralysis. A central lesion also is usually associated with some other symptoms of intracranial disease, often a hemiplegia. The seat of the lesion can often be accurately located. If the facial nerve alone is involved and the sense of taste is unimpaired, the

lesion is in the trunk of the nerve, outside of the skull, or is just within the stylomastoid foramen. If the sense of taste in the anterior portion of the tongue is affected, the lesion is in the Fallopian canal. If complete deafness occurs with the facial palsy, disease in the trunk of the nerve at the base of the brain is indicated, while, if there is associated paralysis of the sixth nerve, the lesion is probably located in the pons.

ETIOLOGY AND PATHOLOGY.—Facial paralysis may be due to a lesion involving any part of the facial nerve-tract from the motor center in the lower Rolandic area of the cortex to the face muscles of the opposite side. If the lesion lies in the cortex or between cortex and facial nucleus in the pons, we have a “supranuclear” facial paralysis. If the lesion involves the nucleus in the pons, we have to deal with a “nuclear” paralysis. If the fibers of the nerve itself be affected, the term “infranuclear” is applied. A supranuclear or central paralysis is usually seen in association with a hemiplegia; the electrical reactions remain unaltered, the upper muscles of the face are but little involved, and voluntary movements are more impaired than is the power of emotional expression.

The peripheral form of Bell's palsy, or facial paralysis, that arising from lesions of the nerve-trunk or nerve-roots in the pons, is one of the most common of the peripheral paralyses. It is more often seen in early middle life, and in men than in women. The great majority of the cases have as their basis a neuritis of the facial nerve, due to exposure to cold. Such cases are sometimes referred to as “rheumatic.” Other causes are in-

jury to the nerve-fibers, as from accidental cutting during surgical operations upon the neck, or from blows, compression, temporal-bone disease, etc.

TREATMENT.—The pathological process underlying the paralysis, when such exists, should be first dealt with. In the common neuritic cases a **mercurial purge** should be given in the beginning, followed by **counterirritation** over the affected nerve-trunk, in the form of a **blister**, the **actual cautery**, or a strong **galvanic current**. The internal administration of **aspirin**, **salicylates**, or **salol**, continued for some days, is advisable. **Potassium iodide** is almost always beneficial, even in cases destitute of syphilitic taint. It should be given in moderate doses, continued for a long time. After subsidence of the acute symptoms **facial massage** and the local application of the **faradic current** in strength sufficient to produce muscular contraction will serve to hasten restoration of power to the paralyzed muscles.

LOCALIZED NEURITIS.

Disorders of the **glossopharyngeal**, or ninth pair of cranial, nerves are attended by perversions of the sense of taste, as well as by abnormalities of common sensation and motion in parts to which the nerve is distributed. The nerve may be affected alone, but is often involved, along with the hypoglossal, in the (nuclear) changes of bulbar paralysis.

The **pneumogastric** nerve, with its extensive distribution and varied functions, gives, when affected by disease, a many-sided clinical picture, the more prominent features being cardiac irregularities and gastric disorders. The nerve is rarely alone in-

involved, but not infrequently participates in the morbid changes of multiple neuritis, or beriberi. It may also be affected from injury, as a result of pressure from a tumor, etc. The tachycardia and acute gastric symptoms pertaining to disease of the pneumogastric nerve have already been referred to under multiple neuritis.

Some of the cases of "nervous" dyspepsia are attributable to disorder of the vagus. Some forms of paralysis of the larynx and pharynx, as well as some of the laryngeal neuroses, depend upon disorder of this nerve.

The **spinal accessory** nerve may be affected by a neuritis, rheumatic or other, or by injuries, tumors, etc. The result is paralysis or weakness of sternomastoid and trapezius muscles. Spasmodic wry-neck is sometimes traceable to spinal accessory disease.

The **hypoglossal** nerve is often involved as a part of a bulbar palsy, or in course of general paresis or other degenerative nervous disease. The prominent symptoms are paralysis and atrophy, with fibrillary tremor in the side of the tongue, with deviation of the tongue toward the sound side.

INFLAMMATION OF SPINAL NERVES.

The noteworthy diseases of the spinal nerves are the general conditions of neuritis, degeneration, etc., already described; the painful affections included under the term neuralgia (*vide infra*) and the affection known as sciatica, now to be dealt with.

SCIATICA.

This is to be regarded as a form of neuritis chiefly interstitial in character, the pathological changes being

located in the nerve-sheath. In severe cases the nerve-fibrils are also affected. The lesion is usually localized at the sciatic notch and near the middle of the thigh, and the pathological alterations shown are those of simple neuritis, previously sketched.

According to Scandinavian observers, "sciatica" is a muscular disorder due to strain. Palpable changes are found at some point in the back of the leg. If, when the pain appears in Lasègue's test, the movement at the hip is reversed a few degrees, the pain stops, but is brought on again if pressure is now made on the tendons of the hamstring muscles, particularly the biceps, thus indicating that the pain arises in the muscles. E. Warburg (*Ugeskr. f. Laeg.*, June 12, 1924).

The malady is most common in middle life, and is seen more frequently in men than in women. The remote or predisposing causes are general malnutrition; rheumatic, gouty, and uric acid diathesis; digestive defects, syphilis, and anything which lowers general vital tone. The exciting causes are exposure to cold, muscular overstrain, and direct injury, as from pressure or blows.

SYMPTOMS.—The characteristic symptoms of sciatic neuritis are pain and tenderness along the course of the sciatic nerve, with weakness and a sensation of stiffness in the muscles. The onset of the pain is usually gradual, it being felt at first only on exertion, but, as it becomes more severe, being constant. It is at times a dull ache; at others a sharp lancinating or acute burning pain. Formication, tingling, and some degree of anesthesia are common. In the later stages there is some atrophy of the calf and other muscles supplied by the sciatic nerve, and in a few in-

stances the disease extends to the lumbar plexus of nerves.

Trophic disorders, as edematous swelling and herpes, are of not infrequent occurrence.

The disease endures for weeks, months, or even years, although eventual recovery is the rule. Most cases last for months. The more acute and severe the initial symptoms, the longer the case will probably last. An obstinate form of neuralgia may persist after the other symptoms of sciatic neuritis are entirely gone. Secondary sciatic neuritis, from pressure of a tumor or a similar cause, can, of course, be relieved only after removal of the cause.

DIAGNOSIS.—As recently emphasized by Alexander, blunders in diagnosis are comparatively frequent. In neurasthenic pain there is a lack of objective symptoms; the pain is constant rather than paroxysmal; it fluctuates with the mood and with insomnia; the attention cannot be diverted from the pain, and the patient begins to groan when the foot is grasped for the Lasègue test. In true sciatica pain is not experienced until the leg is raised to an angle of 45 or 60 degrees. Spondylitis, sacroiliac disease or stretching of the symphysis in a wasting disease or pregnancy, and senile hip-joint disease frequently develop sciatic pain as the first symptom, but the insidious course, the röntgenoscopic findings, and the pain in the hip-joint when the flexed leg is passively moved differentiate the affection. In tabes the pain is generally bilateral and independent of active or passive movements; instead of the Lasègue sign, there is hypotonicity without pains. The writer has never encountered

sciatica in a tabetic nor a case of sciatica traceable to flat-foot alone. The sacral form of multiple sclerosis is hard to distinguish from true sciatica.

Lasègue's sign of sciatica consists in the production of pain when, with the patient in dorsal decubitus, the examiner raises the limb of the affected side with the knee kept in extension. If the sign is absent, except in early cases, the sciatic pain previously complained of is usually of hysteric nature. If the raising of the leg causes pain on both sides, a radicular disturbance is indicated (Chmielewski).

According to Pisani, a pathognomonic sign is afforded by an increase of the abdominal reflex on the affected side, while the reflexes are less pronounced or absent on the sound side. The superior, median, and inferior reflexes should all be tested. The patient lies on his back with his abdominal walls fully relaxed, and the limbs extended symmetrically. This sign is found in over 80 per cent. of all patients.

In several long-standing cases, the source of trouble was found by Enriquez and Gutmann to be located at the lower extremity of the cecum. In all of 3 operated cases, adhesions were found uniting firmly the cecoappendicular structures, which were situated low down, with the posterior parietes. After appendectomy and liberation of adhesions the sciatica disappeared.

To obtain the gluteus sign the writer, with the patient prone, taps on the point of attachment of the gluteus maximus on a level with the second, third and fourth parts of the sacrum. This muscle then contracts, in exaggerated fashion in true sciatica. F. Rosa (*Presse méd.*, June 4, 1917).

Flexion of the big toe on percussion of the tendo Achillis, in disorders of the sciatic nerve, may occur as sole symptom and can thus settle a doubtful diagnosis. Villaret and Faure-Beaulieu (*Presse méd.*, Sept. 13, 1917).

A thorough clinical and X-ray search for structural changes in the lumbar spine and pelvic region should be carried out in every case of sciatic nerve symptoms. Tumors of the lum-

bar spine and pelvic region rarely exist without producing symptoms in the course of the sciatic. When the bone is involved, nerve tissue is destroyed very rapidly. Traumatic separation of the symphysis pubis, as from a forceps delivery, twists one or both sacroiliac joints, with pressure symptoms referred to the sciatic. Because of the proximity of the lumbosacral cord to the 5th lumbar transverse process or to the lateral lumbosacral articulation, fracture of either usually produces enough callus to cause marked sciatic irritation, and occasionally paresis or paralysis. Chappel (*Cal. and West. Med.*, Mar., 1924).

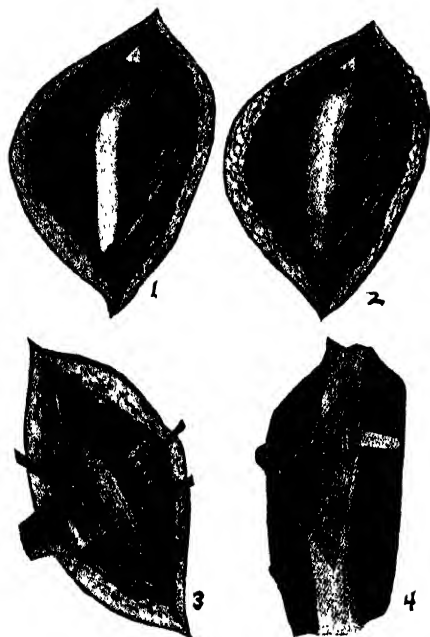
From anatomic investigations and clinical studies of 21 cases, the writers conclude that sciatic pain without obvious cause is a symptom of disturbance in the lower lumbar spine, and that the site of the lesion is most frequently the lumbosacral junction, and the nerve chiefly involved the 5th lumbar. M. S. Danforth and P. D. Wilson (*Jour. of Bone and Joint Surg.*, Jan., 1925).

TREATMENT.—In the treatment of sciatica the first requisite is absolute and complete rest of the limbs, all movements which give the least pain being scrupulously avoided. Simply confining the patient to bed may answer in many cases, but in the aggravated forms placing the limbs in splints is advised; or, sand bags may be used to maintain immobility of the limb.

Hot applications, as hot poultices, superheated air, etc., are grateful in relieving the pain, while occasionally ice is more useful. Counterirritation by the actual cautery gives great relief sometimes. A strong galvanic current is always of service; the anode should be placed over the sciatic notch and the anode at the foot, and the current thus passed for 10 minutes daily.

Intravenous injections of **phenol** (Bacelli's method), 1:1000 solution, used in 11 cases, some of several years' standing. From 10 to 60 injections were required. Rosi (Policlinico, Oct. 13, 1912).

Marked improvement in 2 cases after a few daily subcutaneous injections of 1 c.c. (16 minims) of 1:1000 **epinephrin** solution. Gaisböck (Med. Klinik, Mar. 16, 1913).



1, Sciatic nerve as it emerges from the sacro-sciatic foramen unmodified; 2, sciatic nerve after intraneural injection of salt solution; 3, sciatic nerve after stripping off the perineurium, without adhesions; 4, sciatic nerve with adhesions extending to the perineurium. (*Heile*.)

(Berliner klinische Wochenschrift.)

Cold water injected into the muscles gives great relief. **Acupuncture** is frequently of great value. Where local remedies fail, the internal administration of **coal-tar analgesics** or **morphine** may be necessary.

In view of the rheumatic tendency in these cases, **salicylates** should be tried out. **Potassium iodide** and **nitroglycerin** may be effective in arteriosclerotic patients.

In a case of acute rheumatic sciatica, an intravenous injection of 1.5 Gm. (23 grains) of **sodium salicylate** in 75 c.c. (2½ ounces) of distilled water was given. There was a sharp febrile reaction with pain in the limbs, but by the next day all symptoms, including the sciatica, had disappeared. In another case, in which the patient had been bed-ridden for months on account of the severe pain, and after failure of treatment by the mouth, improvement followed an intravenous injection of 3 Gm. (45 grains) of sodium salicylate, and after a second dose on the succeeding day the sciatica was completely relieved. Weill-Hallé and Chabanier (Bull. Soc. méd. des hôp. de Paris, July 27, 1922).

In a case of obstinate sciatica with lumbago, the blood Wassermann was found positive, but the spinal test negative. Permanent recovery took place, however, under **antisyphilitic treatment**, thus suggesting the identity of the causative process as a syphilitic meningomyelitis. C. Gram (Ugesk. f. Laeger, Mar. 26, 1925).

Various non-operative mechanical measures have been deemed serviceable by certain observers.

Heermann pulls on the leg of the reclining patient, exerting about as much force as for pulling off a boot. If this relieves the pain, he applies extension systematically, raising the extended leg once or twice a day to the point borne without special pain and then applying extension to the foot with the leg resting on an inclined plane. This is repeated cautiously once or twice a day for 5 to 30 seconds. This **stretching** is supplemented by stretching the leg backward for a few seconds as the patient lies on the side. The ordinary measures are also applied, but the nerve stretching often proves successful alone.

A simple maneuver for the relief of sciatica, successful in the author's own person as well as in other cases, described. It was conceived by analysis of movements made by him when seized with a severe attack while riding on horseback, whereupon these

movements had brought abrupt relief from the pain. Adapted for clinical use, the maneuver is as follows: (1) Lie flat on a hard mattress; (2) straighten the affected leg, applying the sole of the foot against the foot of the bed; (3) turn the foot and, at the same time, the whole limb up to the hip-joint, in the direction of supination, while pressing hard with the heel against the foot of the bed; (4) twist the upper part of the body in the opposite direction, at the same time straightening out the trunk and raising the shoulders as much as possible. The whole limb is thus extended to the utmost and twisted from hip to heel in one direction while the trunk is extended and twisted in the opposite direction. The relief is sometimes as sudden as in reduction of a dislocated shoulder by Kocher's method. Jaquerod (Rev. méd. de la Suisse rom., Apr., 1924).

The diet should be liberal and the general bodily state improved as much as possible by **tonics** and **hygienic measures**.

Nourishing diet, with fats predominating, advised. Milk, cream, eggs, butter, marrow, bacon, and oils to be given, with frequent feeding between meals, but meats to be eaten sparingly. Half an hour before each meal, give a large cup of **hot water** containing a **glycerophosphate**. Hunt (Med. Record, June 28, 1913).

In the later stages of the malady **electricity** and **massage** should be used systematically, as they shorten the period of convalescence. **Dia-thermy** and the **static wave current** have, in particular, proven useful.

Frequent application of **dry cupping glasses** by the patients themselves is advocated by Orb. **Very light friction**, carefully applied by the physician himself, avoiding the most painful spots, is sometimes very useful.

Injectations of **saline solution** (up to 100 c.c. or more) or other solutions

into the sciatic nerve have given good results in a large proportion of cases. The saline solution is introduced either pure or with an anesthetic. **Perineural injections** are recommended by Cathelin, Sicard, and many others.

According to Sicard, where an acute attack, in spite of the usual measures, persists longer than 10 to 14 days, **sulphur baths** or **hot carbon dioxide baths** (102.7° to 104° F., lasting 20 minutes) should be employed, or **heat** applied in other ways. If ineffective, he counsels injections of **saline solution** and **air**: 1. Injection of 800 to 1000 c.c. of air, filtered through cotton, under skin on outer aspect of leg. 2. Injection of 60 to 80 c.c. (2 to 2½ fluidounces) of 0.8 per cent. **salt solution**, with 0.01 to 0.02 Gm. (⅙ to ⅓ grain) of **procaine** added, just below sacrosclatic notch, as close to nerve as possible. 3. Injection of 10 to 20 c.c. (2½ to 5 fluidrams) of **salt solution**, with 0.01 Gm. (⅙ grain) of **procaine** into epidural space of inferior lumbar region, needle being passed in and up through coccygeal notch; preliminary anesthesia of course of injection with procaine. 4. Where there is very severe pain and contractures of lumbar muscles, injection of 10 to 15 c.c. (2½ to 3¼ fluidrams) of salt solution between third and fourth lumbar vertebræ into the epidural space. Injections to be repeated at intervals of three or four days, substituting 1 to 1.2 per cent. for 0.8 per cent. saline. Two to 5 series of injections cure obstinate cases.

Recent and mild cases are usually cured by 1 injection of 15 to 30 cc. (½ to 1 ounce) of 1 per cent. **quinine** and **urea hydrochloride** solution into and in the vicinity of the nerve, while long-standing cases may require 4 or 5 injections at intervals of 2 or 3 weeks. Attempt is made to inject 5 c.c. (80 minims) of the solution directly into the substance of the nerve and the remainder in its immediate vicinity. Lying on the well side, the patient has the thigh and leg on the affected side half flexed. At a point somewhat lateral to the midpoint of a line joining the ischial tuberosity and

great trochanter, a wheal is first made with a fine needle, and a larger needle, 4 or 5 inches long and of 18 gauge, is then introduced slightly upward and inward. If it strikes the nerve the usual pain shooting down the leg is felt, while to the operator it feels as if the needle had passed into a rubber tube. If the neck of the femur is struck, the needle is partly withdrawn and started in new directions until the nerve is located. A. F. Hertzler (*Amer. Jour. of Surg.*, Apr., 1924).

In severe cases the writer had good effects from perineural injections of 10 c.c. (2½ drams) of distilled water containing 4 Gm. (1 dram) of antipyrin and a little procaine. Höglér (*Wien. klin. Woch.*, Jan. 15, 1925).

Epidural injections have been recommended by Blum and others for cases in which perineural injections fail.

Glimm obtained prompt and permanent cure of sciatica with **epidural injections** of about 20 c.c. (⅔ fluidounce) of physiological salt solution or a weak anesthetic. The best results were obtained with this amount of Schleich's No. 2 solution, which proved effectual in 5 of 7 inveterate cases.

Twelve cases of sciatica treated with **epidural injections of procaine**. Seven were permanently cured. One cg. (⅓ grain) of procaine, 0.25 Gm. (4 grains) of sodium bicarbonate, and 0.5 Gm. (7½ grains) of sodium chloride are dissolved in 100 c.c. (3½ fluidounces) of cold distilled water. This solution is injected into the sacral notch between the tubercles. In 15 or 20 minutes after the injections all the symptoms of sciatica disappeared, but the writer left the patients in bed for a few days. Langbein (*Deut. med. Woch.*, xxxix, 20, 1913).

Epidural injections used in 48 cases in which no definite causal factor could be found. Removal of foci of infection was also carried out in a large percentage. Permanent cure resulted in 29 per cent.; improvement permitting return to work in 37 per cent., and no

permanent benefit in 34 per cent. W. O. Ott (*Ann. of Surg.*, Aug., 1922).

Epidural injections of 25 per cent. solution of C. P. magnesium sulphate to the amount of 1 c.c. (16 minims) per 20 kilos. (44 lbs.) of body weight found valuable in the painful attacks of 7 acute and 3 chronic cases. Several injections of 2 or 3 c.c. are also made at painful points along the course of the sciatic, the total amount used in all the injections being 10 c.c. (160 minims). The effect is practically a physiologic section of the cord, and there may be slight disturbance of the sphincters and respiration. The analgesic effect begins in 1½ to 3 hours, is more pronounced the next day, and persists 2 to 4 days. Garofeano and B. Labin (*Arch. méd. belges*, June, 1923).

According to Jassanetzky-Woino, complete anesthesia of the sciatic nerve can be brought about by means of a 2 per cent. novocaine-adrenalin solution, 10 minims being injected. The point where the nerve can be easily and safely injected corresponds to the junction of a horizontal line passing through the top of the great trochanter and a vertical line through the margin of the tuberosity of the ischium. In 3 out of 20 cadavers the horizontal line was from 1 to 1.5 cm. too high. In all the others the junction of these two lines was exactly at the point where the nerve, immediately after making its exit from the great sciatic foramen, lies directly on the bone.

The most satisfactory method of treatment comprises **absolute rest** in bed, **warmth** along the nerve and specially in the gluteal region, and large doses of the **salicylates** during the early stages. If the attack does not respond, the writer injects 100 to 150 c.c. (3⅓ to 5 ounces) of **saline solution** into the region of the sciatic nerve at a point 1 inch to the outer side of the junction of the inner ⅓ with the

outer $\frac{2}{3}$ of a line drawn between the sacrococcygeal articulation and the lowest point of the posteroexternal border of the great trochanter. From 3 to 5 such injections may be required at intervals of 2 days before there is permanent relief. A second method is the injection of 60 to 80 c.c. (2 to 2 $\frac{2}{3}$ ounces) of **warm sterile saline solution** into the epidural space through the superior sacral foramen. The first 10 to 20 c.c. (2 $\frac{1}{2}$ to 5 drams) of the saline should contain a small amount of **adrenalin** and 0.125 Gm. (2 grains) of **procaine**. I. Strauss (Jour. Amer. Med. Assoc., Dec. 15, 1917).

The injection treatment is the simplest and least radical, but it is best to use **combined nerve trunk injection and epidural injection**. O. Wiedhopf (Beit. z. klin. Chir., cxxxii, 523, 1924).

The **X-rays and autogenous vaccines** have been tried with some degree of success.

Gratifying relief of pain in 10 cases, some severe, by **X-ray** treatments over the 4th and 5th lumbar and first 4 sacral vertebrae, the rays slanting down to the nerve and being filtered through 1 to 3 mm. of aluminum. A dose of 3H seemed sufficient. The intervals between treatments were 10 to 20 days. Japiot (Lyon méd., Feb. 25, 1921).

Report on 33 cases, of 1 to 3 years' standing, and bilateral in 8. The nerve-roots were irradiated between the 12th dorsal vertebra and the lower part of the sacrum, while in the presence of tenderness in the gluteal region, this was also included. A 4 mm. aluminum filter was used, and the dose was $\frac{2}{3}$ skin unit. Where 1 treatment did not suffice, the procedure was repeated in 2 or 3 weeks. Complete recovery in 55 per cent.; improvement in 30 per cent.; 15 per cent. unimproved. Kahlmeter (Hygiea, Jan. 15, 1925).

Surgical measures, such as **nerve stretching, splitting the sheath, etc.**, may be tried in refractory cases.

Eight out of 10 cases rebellious to medical measures were cured by **freeing the nerve from adhesions**. The

writer exposes it below the gluteus maximus by a 4 to 5 inch longitudinal incision, hooks it up, and carefully removes all adhesions from the sacrosciatic notch to about the middle of the thigh. Care is taken to preserve the branches to the hamstring muscles. J. M. Renton (Brit. Med. Jour., Apr. 16, 1921).

The writer cures all obstinate cases by exposing the nerve at its point of emergence, mobilizing it as far up as possible, and **stretching** it slightly. Graff (Beit. z. klin. Chir., cxxvi, 287, 1922).

The trouble is sometimes due to adhesion of fibers within the nerve itself, to a fibrosed epineurium, or to pressure from an abnormal network of veins over the nerve trunk. Adhesions between epineurium and perineurium can be broken by lifting up the former with fine forceps. Internal adhesions are relieved by **intra-neural injection** of 30 to 50 c.c. of 0.5 per cent. **procaine** followed by **injection** of 100 to 200 c.c. of **saline solution**, greatly distending the nerve trunk as well as detaching the adherent epineurium. Where pathologic conditions exist at the origin of the nerve, **section of posterior roots** may be necessary. Heile (Deut. Zeit. f. Chir., Sept., 1922).

NEURALGIA.

DEFINITION AND VARIETIES.—Neuralgia is a functional or mild neurotic disorder of the sensory nerves or their centers, characterized, as the name indicates, by pain. The affection may be idiopathic—depending upon some functional disturbance alone, or it may be symptomatic—due to some organic disease of the nerve or to some disease or pathological state outside of the nervous system, such as neuritis, anemia, and toxemia. The tendency of later years has been to diminish the number of idiopathic neuralgias by the discovery of organic disease with demonstrable changes in nerve-trunks.

Neuralgias are classified, according to their causes, as "neuritic," "toxic," "gouty," "rheumatic," etc.; or according to their location, as "trigeminal," "sciatic," "intercostal," "cervico-occipital," etc. The general features of the disorder will be first discussed, and after these the more important clinical varieties will be briefly described.

SYMPTOMS.—Pain is the chief and characteristic symptom, the onset of pain being sometimes preceded by soreness and stiffness in muscles and tissues of the affected part, sometimes developing suddenly and without warning. The pain is intermittent or paroxysmal, of a darting, stabbing character, accompanied sometimes by burning and tingling sensations. There is usually tenderness over the entire nerve-trunk, with certain "painful points" at which the tenderness and pain are greatest. The paroxysms of pain may occur only at long intervals, but usually, for some hours, they occur every few minutes; in aggravated cases they may be nearly continuous for hours or days. In occasional cases there may be some pain continuously for months or even several years. In some instances the pain is greatest at a certain time each day, especially, though not always, in malarial cases.

Trophic and vasomotor disturbances in the affected area, such as coldness, herpetic or urticarial eruptions, falling out or changes in color of the hair, etc., are occasionally seen. In some forms of neuralgia twitching or spasm of adjacent muscles accompanies the paroxysms.

Attention directed to the frequent presence of small intradermal nodes in patients suffering from neuralgia, the

process concerned being sometimes known as *cellulitis*. The author considers it the fibrous end-result of a congestive condition of the subcutaneous cellular tissue, earlier manifested in hypertrophic change, new vessel formation, and perineuritis of the cutaneous nerves. The neuralgia and cellulitis are due to the same original cause. In these cases there is tenderness at the points of emergence of the nerves. The neuralgia is due to pressure, possibly due to vascular ruptures producing interstitial hemorrhages in the nerves, followed by chronic infiltration. Many cases of neuralgia can be cured or improved by **massage**. Wetterwald (Prog. méd., Feb. 4, 1922).

DIAGNOSIS.—The diagnosis of neuralgia is simple, the presence of the characteristic pain being sufficient. The only practical difficulty is in distinguishing between neuralgia and neuritis, and here, since the conditions shade into one another, it may be impossible to draw a sharp dividing line. Generally speaking, the pain in neuritis is more constant in location than is the pain of neuralgia; it does not shift nor dart from one nerve to another; there is in neuritis much more muscular weakness, stiffness on movement, and relaxation of tissues, and absence of the history of repeated attacks.

In the diagnosis between myalgia and neuralgia, Peritz stresses the tenderness of one or more muscles in myalgia, with hyperalgesia of the skin over these tender muscles; injection of a little sterile salt solution into a muscle proves painful if it is inflamed, otherwise not; frequently patients with myalgia complain of paresthetic symptoms; rather often the affected muscles show some weakness; the character and topography of the pain are likewise different in the two conditions.

Rheumatism of the vertebræ and tuberculous bronchial lymph-nodes may induce sharp spinal pains simulating other troubles. The pain and hyperesthesia

with these affections are always bilateral. The patient may not be aware of this bilateral character,—usually not,—but it can be determined by delimiting the area with the needle and studying the character of the pain, which is always typical of true neuralgias. The zones of hyperesthesia are abnormally sensitive to contact, to pressure, and to temperature. The “pressure points” are also excessively tender. Zuelzer (Berl. klin. Woch., Sept. 8, 1913).

ETIOLOGY.—Neuralgia is a disease of middle life, rarely affecting children and rarely occurring in old age. It is somewhat more frequent in women than in men; more frequent in cold than in warm weather; more frequent in cold and damp climates than in dry and warm localities.

Members of neuropathic families are more liable to the disease than are persons of good nervous heredity. The immediate exciting causes are anything which lowers general nerve tone and any toxic agent or disease attended by toxemia, such as anemia and general cachectic states, malaria, infectious diseases, autogenous poisonings, diabetes, lead poisoning, etc.

Report of 53 cases of neuralgia due to excessive smoking. There were 31 cases of sciatica and 22 of brachial neuralgia. Diffuse pains, not restricted to individual nerve areas, were represented by 110 cases. The nature of these latter is obscure, as in some cases an arthropathy seemed to be present. The condition termed by Erb *dyskinesia intermittens angiosclerotica* is abundantly recognized by its sponsor as occurring much more frequently in heavy smokers than in any other class of people. It is very largely a tobacco angioneurosis. Von Frankl-Hochwart (Deut. med. Woch., Dec. 14, 1911).

Exposure to cold may precipitate attacks in those predisposed, as may reflex irritations from disease of eyes, ovaries, abdominal organs, carious teeth, etc.

Case in which the patient complained bitterly of pain back of the eye, the vision of which was slightly affected and the visual field somewhat contracted. The papilla was rather congested. Examination revealed a gold-capped tooth, the left upper second molar, which was sensitive and had been recapped several times by different dentists during the past year. Extraction of the tooth was advised and performed, when a dental spud was found extruding from its posterior root about $\frac{1}{16}$ inch. The pain back of the eye was completely relieved, the vision improved to normal, the blurring disappeared, and the visual field was nearly normal two days after the extraction of the tooth. H. V. Wuerdemann (Ophth. Record, Nov., 1913).

Where hereditary predisposition is very strong the affection may develop without discoverable cause. The neurasthenic and hysterical are particularly prone to suffer from neuralgia.

In many cases of neuralgia, the true “functional” or idiopathic cases, no pathological alterations in the nerve-fibers, cells, or ganglia can be detected, the presumption being that the pain is due to malnutrition or toxemias of a degree too slight to cause alterations of structure. In other cases the nerve-trunks are swelled and tender, and in most such cases the pathologicoanatomical changes are those of a mild interstitial neuritis.

TREATMENT.—The first indication is **removal of the cause**, when such is discoverable and can be removed. **General tonic and hygienic**

treatment is always advisable, as any improvement in vital tone and blood quality gives measurable relief from idiopathic neuralgia. **Removal from an unhealthy climate** often gives relief. **Iron, arsenic, strychnine, cod-liver oil, and phosphorus**, singly or in combination, are the tonics most used. **Quinine**, at one time much lauded as a specific for some forms of neuralgia, is apt to prove disappointing.

Case of trifacial neuralgia of fourteen years' standing which had resisted all the usual remedial means, including resection of the sensory root of the nerve and the injection of cocaine, and in which subcutaneous injections of **quinine and urea hydrochloride** brought apparently permanent relief. H. Crenshaw (Therap. Gaz., Dec., 1912).

Records of 5 cases of trifacial neuralgia (1 case being multiple neuritis plus trifacial neuralgia) in which the treatment consisted of **strychnine** exhibited in large doses. All of these cases were due to infection, which seems to be the important indication for the exhibition of strychnine. The strychnine treatment was given by mouth or hypodermically in $\frac{1}{40}$ - to $\frac{1}{30}$ - grain (0.0016 to 0.0022 Gm.) doses hourly for four hours morning and evening. Orbison (Calif. State Jour. of Med., Oct., 1913).

Local applications are sometimes helpful in the milder forms.

For the local treatment of neuralgia, the following liniment is recommended:—

℞ *Chloroformi* f℥ss (15 c.c.).
Ætheris f℥iss (45 c.c.).
Alcoholis f℥iv (125 c.c.).
Camphoræ ℥ij (8 Gm.).
Tincturæ opii ℥L (3 c.c.).

M. et ft. linimentum.

A square piece of flannel should be moistened with the liniment, placed

over the seat of pain, and covered with some impermeable material.

In pains at the anus not accounted for by a fistula or rectal lesion the following liniment may be rubbed over the part several times a day:—

℞ *Extracti belladonnae*
foliorum 3ss (2 Gm.).
Chloroformi f℥ss (2 c.c.).
Glycerini f℥ss (15 c.c.).

M. et ft. linimentum.

In periorbital neuralgia and ophthalmic migraine the writer uses the following ointment:—

℞ *Mentholis* gr. xiiij (0.85 Gm.).
Cocainæ gr. iv (0.25 Gm.).
Chlorali hydrati. gr. iiss (0.15 Gm.).
Petrolati gr. lxxv (5 Gm.).

M. et ft. unguentum.

Sig.: Rub ointment over the seat of pain and cover with oiled silk.

Galezowski (Paris médical, May 31, 1913; N. Y. Med Jour., Dec. 6, 1913).

The systematic use of electricity, long continued, is one of the most valuable means at our disposal for the permanent relief of neuralgic pain, the **galvanic and high frequency currents** giving the best results.

Use of the **X-rays** and the **ultra-violet rays** has also been lauded.

Application of **X-rays** to the corresponding nerve-roots gives good results in brachial or trigeminal neuralgia or neuritis, provided the condition be due to a true radiculitis or a lesion compressing the nerve-roots, and not to peripheral involvement. Zimmern, Cottenot, and Dariaux (Presse méd., June 25, 1913).

The **ultra-violet rays** recommended in both neuralgia and neuritis. They relieve the pains, and may cure in some instances. Lichnitzki (Paris méd., Dec. 20, 1924).

Of remedies for the relief of the paroxysms of pain the **coal-tar derivatives** stand first. **Gelsemium** also is a valuable antineuralgic agent, as

are **ether**, **valerian** (these last two often in combination); **aconite** or its active principle, **aconitine**; **cannabis Indica**, and **cimicifuga**. **Alcohol** given internally oftentimes affords relief, but it is a dangerous remedy and should be prescribed with caution. **Nitroglycerin** has been found useful in cases of facial neuralgia.

If 5 to 10 drops of **guaiacol** are gently rubbed into the skin over the painful spot, the neuralgic pain will cease at once, no matter of what character the neuralgia may be. A. Brodnax (Wisconsin Med. Recorder, p. 228, 1900).

One-fourth, $\frac{1}{8}$, or even $\frac{1}{10}$ grain (0.015, 0.008, or 0.006 Gm.) of Merck's medicinal **methylene blue**, in watery solution, hypodermically near the seat of pain or near the spinal source of the affected nerve is generally sufficient. Using these small doses, two points of injection may sometimes be advisable at the same sitting. A. de Voe (Medical World, Sept., 1902).

Chloroform is the nearest approach to a specific in the treatment of neuralgia. The method is devoid of any untoward effects, both immediate and remote. Chloroform injected locally has no systemic effects, but a local anesthetic effect. Superficial injections often act with certainty, even when the pain seems to be deep seated. S. Ormond Goldan (N. Y. Med. Jour., June 13, 1908).

The writer has obtained good results in 16 cases of exceptionally severe trigeminal neuralgia and also in 100 moderate cases by treatment with **aconitine** and **vigorous purgation**. The aconitine seems to have actual specific efficacy in trigeminal neuralgia. He prefers to give it in the form of 8 or 10 pills containing a maximum of 0.002 Gm. ($\frac{1}{32}$ grain) for the daily dose. It is supplemented with **calomel**, 15 grains (1 Gm.) in 10 doses in ten hours (0.1 Gm.— $1\frac{1}{2}$ grains—per dose), continu-

ing afterward with a laxative water three times a day. In giving the aconitine he inquires constantly for signs of intoxication, paresthesia in tongue, lips, or hands, mostly in the ulnar region, but has never observed anything of the kind, probably on account of the vigorous purgation which he regards as the greatest advance in the treatment of neuralgia in the last quarter-century. Fuchs (Med. Klinik, July 18, 1909).

Since preparations of **aconitine** have become reliable, this agent can be advantageously employed in neuralgias of the fifth pair, especially when all other antineuralgics, such as morphine, quinine, antipyrin, pyramidon, phenacetin, etc., fail. It is given in doses of $\frac{1}{20}$ mg. every two or three hours until the desired effect is obtained—1 mg. ($\frac{1}{65}$ grain) within twenty-four hours never to be exceeded. In facial and secondary neuralgias aconitine acts as a specific in allaying the pain; at the same time the removal of the causative factor must not be overlooked. During the dosing, the patient must be watched for dryness of the mouth, tickling sensation in the extremities, —a very characteristic phenomenon, —and paresthesia of the lips and tongue, these symptoms indicating diminution in dosage or extension of the intervals of administration. H. Versluysen (Revue trimes. belge de stomat., June, 1910).

Case of severe trifacial neuralgia in which, all ordinary measures finally proving unavailing, 2 injections of the following solution were made into the infraorbital canal on two successive days:—

\mathcal{R} *Sodii salicylatis*. gr. viiss (0.5 Gm.).
Cocainæ hydro-
chloridi gr. $i\frac{1}{4}$ (0.075 Gm.).
Aquæ destillatæ f3iiss (10 c.c.).

M. et ft. solutio.

The injections were administered slowly with a 2-c.c. ($\frac{1}{2}$ fluidram) syringe, under local anesthesia of the skin with **ethyl chloride**, the infraorbital foramen having first been

located at the junction of the inner third and outer two-thirds of the lower margin of the orbit, 5 mm. below a slight bony elevation palpable with the finger. Relief from pain had been maintained 6 months later. Monestié (*Jour. des sci. méd. de Lille*; *N. Y. Med. Jour.*, Apr. 26, 1913).

Magnesium chloride recommended for dull aches of the sort that are made worse by draughts or cold, damp weather. H. S. Weaver (*Jour. of Ophth., Otol. and Laryng.*, Mar., 1922).

When all other remedies fail, **morphine** hypodermically may justifiably be used, but there is great danger in these cases of initiating the habit.

For severe neuralgia, **castor oil**, 1 to 2 fluidounces (30 to 60 c.c.) 3 or 4 times daily, has been extolled by Waxham. In some cases smaller amounts sufficed. After the first 2 or 3 doses it usually loses its cathartic effects. The constitutional effect is the effect that is desired.

According to Reyburn, **ergot** is useful in the chronic neuralgia of overfed women in the higher walks of life who take little or no exercise. A fluidram (4 c.c.) of the fluidextract 3 times a day, with insistence on **exercise** and a reduced diet, acts well in these cases.

Case of severe neuralgia of the right ophthalmic nerve, of 5 years' standing, in a man of 37, in which **ionization** with a 3 per cent. **sodium salicylate** solution brought lasting relief after 3 sittings at 3-day intervals. The positive electrode was a towel dipped in distilled water and placed over the back of the neck. The active electrode was placed over the pharyngomaxillary region. The current was increased at successive sittings from 20 to 40 and then to 70 ma., and the duration from 20 to 35 and finally 50 minutes. Jouin (*Jour. de méd. de Paris*, Dec., 1919).

In the case of a child of 8 with a history of oxyuris infestation and influenza who developed attacks of *peri-orbital neuralgia* on the left side, cure followed ingestion of 0.5 Gm. (7½

grains) of **peptone** for 2 months. Nageotte-Wilbouchewitch (*Bull. Soc. de péd.*, Jan., 1922).

Use of **atropine** internally in small doses for 3 or 4 weeks advised. A 0.1 per cent. solution is used, beginning with 3 drops 3 times a day and increasing at intervals of 5 days up to 8 drops. The object of this treatment is to reduce the excessive irritability of the sympathetic nervous system. Kulenkampff (*Münch. med. Woch.*, Feb. 6, 1925).

Acupuncture, injection of **water** or **saline solution** beneath the skin, and active **counterirritation** may also be used with some hope of benefit.

In all neuralgias except those due to surgical conditions, the writer recommends **subcutaneous injection** of 50 to 100 c.c. of **oxygen gas**, at a rate not exceeding 30 c.c. per minute and avoiding injection into a blood vessel. After withdrawal of the needle a collodion dressing is applied to seal the puncture. Bolognini (*Gazz. degli osped.*, July 31, 1921).

In neuralgia of the *superior laryngeal nerve*, the author found injections of **alcohol** into the trunk the only efficient measure of many tried, as well as the least dangerous. Halphen (*Bull. Soc. méd. des hôp. de Paris*, Feb. 8, 1924).

In severe and obstinate cases the question of surgical interference may arise, the usual resources being **nerve stretching** and **excision** of a portion of the **nerve-trunk** or of its **ganglion**. These procedures always give temporary relief or respite from pain for some months, but unless there has been total destruction of the affected sensory neurons, as by **removal of the Gasserian ganglion**, the pain is liable to return as the nerve-fibers regenerate. This is referred to under the next heading, the form for which operative procedures are usually necessary.

The author resorts to a species of **crushing of nerves** subject to neural-

gia, at their points of emergence. Holding the patient's head firmly against his own chest with his left arm, he makes strong pressure on the painful point with his right forefinger for $\frac{1}{2}$ to 1 second, 10 times in succession, at 1 second intervals. For 4 to 6 days this causes extreme pain. A second series is then carried out after a 2-day rest. Four to 6 series will sufficiently crush the nerve and cure the neuralgia, even in long standing cases. Janowski (Presse méd., Aug. 7, 1920).

Where motion of the nerve is the source of pain, its liberation is indicated. In 12 cases of so-called *epicondylitis* and 7 of *styloiditis*, in which the pains were severe, persistent and rebellious to all usual measures, cure was immediate and complete when the inflamed or irritated nerve was simply shifted to a more sheltered position, putting an end to its rubbing against the condyle or styloid process. Fisher (Arch. f. klin. Chir., cxxv, 749, 1923).

In 10 patients with *epigastric neuralgia* resembling the pains of gastric ulcer, marked relief followed injections of **procaine** into the painful spot. The addition of **alcohol** cured 2 others, while 5 proved refractory to all measures until relieved by **excision** of the **painful spot** or seat of the neuralgia. In 2 cases asthma accompanied the attack, and in 4, a tendency to neurasthenia was manifest. Subsidence of the pain after injecting **procaine** differentiated the neuralgia from organic disease. Philippsthal (Deut. med. Woch., Sept. 28, 1923).

In even quite severe cases the pains are liable to subside spontaneously in old age, or frequently after the climacteric in women.

Pelvic neuralgia or neuritis frequently arises from organic changes in the female genital organs, and may persist after correction of the primary tubal, ovarian or uterine disturbance. Frequently it confuses the clinical picture. The patient winces when pressure is made over the tender points in

the course of the nerves concerned. The treatment of such neuralgia consists of **rest in bed**, local application of **heat**, and irrigation of the **vagina** with 30 to 40 liters of water at 40 to 45° C. (104 to 113° F.). **High frequency** treatment is also very useful; of 10 patients receiving a full course of it 7 were cured and 3 greatly improved. Hauch (Ugesk. f. Laeger, Nov. 5, 1925).

NEURALGIA OF SPECIAL BRANCHES.

Neuralgia of the Fifth Pair—Tic Douloureux.—Neuralgia of the fifth pair of cranial nerves is also known as trifacial neuralgia, facial neuralgia, etc., and likewise as *tic douloureux* when the pain is extremely severe and attends spasm of the facial muscles.

Neuralgia of the fifth pair is more frequent than all other forms of neuralgia combined, and is, from a clinical standpoint, the most important of the forms of neuralgia with which the physician has to deal, this nerve seeming peculiarly susceptible to functional and organic disorders as a consequence of the complexity and highly differentiated character of its structure and connections.

All three of the branches are seldom affected simultaneously. The ophthalmic branch is that most often involved, giving rise to neuralgic pain in the eye and brow ("brow ache") with an especially painful point at the supraorbital notch. In some cases the pain is especially intense in the eyeball. When the infraorbital branch is involved there is the usual pain in the area of distribution of the nerve, and a marked tender point at the infraorbital foramen. A toothache-like pain in upper teeth is common. In neuralgia of the inferior dental branch the pain is often diffuse, extending

from the temporal region over the side of the face to the chin, with pain in the lower teeth and side of the tongue, the last mentioned being, in some cases, the situation of greatest intensity.

In severe forms of pain involving any branch of the fifth nerve the pain may in lesser degree extend to the other branches. In all forms of facial neuralgia trophic disorders, in particular herpes, may occur. When the pain in facial neuralgia is very intense and markedly paroxysmal, with reflex facial muscular spasm accompanying, we have the form known as "tic douloureux": the most distressing and intractable form of nerve-pain. The general symptomatology and causation, as well as therapeutic indications, of neuralgia in general apply to the facial form.

Correct diagnosis is important, since occasionally, in spite of a technically perfect operation, as proven by complete anesthesia of the 5th nerve distribution, pain persists. Nearly always the condition confounded is Sluder's nasal neuralgia. For differentiation, the best method is to inject one of the affected branches with alcohol; if this temporarily relieves the pain, a true tic douloureux exists; if not, cocaineization of the sphenopalatine ganglion, as devised by Sluder, as a rule clears up the diagnosis. Other conditions simulating tic douloureux are inflammatory conditions about the face and jaws, infected or impacted teeth, tumors on the jaws or gums, retropharyngeal tumors, or intracranial tumors pressing on the Gasserian ganglion. None of these is difficult to recognize except the last, the evidences of which are constant pain in the 5th nerve distribution, paralysis of the motor branch, and anesthesia or hypesthesia. Sachs (Ill. Med. Jour., Feb., 1924).

Treatment.—If any cause of the neuralgia can be found by careful ex-

amination of the nasal passages, mouth or eyes, it should be removed.

Aside from this, improvement in general health should be sought.

For the relief of the acute pain morphine may be effective, but it should not be employed until the coal-tar analgesics, aconite, etc., have been given a trial. A mixture of the ointments of opium and belladonna may be tried locally. Benefit may also result from the salicylates.

Attention called to the value of trichlorethylene, which seemed to paralyze the sensory fibers of the nerve. Out of 20 cases, 5 were cured and 6 improved. The patients inhaled 10 to 20 drops of the drug from cotton once or twice daily. Magunna (Berl. klin. Woch., Mar. 25, 1922).

The continued hypodermic use of strychnine has given favorable results in preventing return of the paroxysms. As advocated by Dana, the dosage is gradually increased, in the course of 10 to 20 days, from $\frac{1}{30}$ to $\frac{1}{5}$ or $\frac{1}{4}$ grain (0.002 to 0.012 or 0.015 Gm.). As adjuvants to the injections, rest in bed, a light diet, potassium iodide, iron and diluents are to be used. As the pain subsides, massage and vibrations to the tender area and sensitive points may be useful.

Having observed that attacks of severe trigeminal neuralgia developed always from 3 to 5 hours after eating, thus suggesting some kinship with alimentary anaphylaxis, and after failure of other measures, the writer obtained a cure under dieting and daily doses of 1.8 Gm. (28 grains) of peptone for 2 weeks. Robert (Prensa med. Argent., July 10, 1924).

Indoxyluria was observed in $\frac{1}{3}$ of all cases of trigeminal neuralgia. Where alkaline mineral waters increase the indoxyluria, the latter is taken to be of intestinal or hepatic

origin; otherwise, it may be due to suppurative foci or disturbed metabolism. Severe cases recovered under a **vegetable diet and liver organotherapy**. Juarros (*Siglo med.*, Jan. 31, 1925).

In old persons **nitroglycerin** in full doses has sometimes reduced the frequency and severity of the attacks.

Occasionally the **galvanic current** proves valuable. With the positive pole over the affected area, the current (usually 3 to 10 ma.), beginning from zero, is slowly increased until it is felt as warm, then gradually decreased, the entire sitting occupying about ten minutes. Administration of **cocaine**, **chloroform** or **aconite** by **cataphoresis** has sometimes given relief for many hours.

Success in 15 cases of facial neuralgia, with marked improvement in 9 cases, from **aconitine ionization**, applied every day or every other day from 10 to 80 times, each session lasting 45 minutes. The positive electrode was moistened with a solution of aconitine nitrate, 0.25 mgm. ($\frac{1}{200}$ grain) to 125 c.c. (4 ounces) of water. Barré (*Médecine*, June, 1923).

The **X-rays** have also given favorable results.

Marked benefit was obtained in cases of occipital, trigeminal and lumbar neuralgia and in meralgia paresthetica from radicular **X-rays**. Excepting the cases of facial neuralgia, particularly those of the tic douloureux type, the results obtained were remarkably constant. They were especially rapid and complete in neuralgia of the brachial plexus. Only rather small doses of the rays need be used; 1 or 2 applications averaging three H units, with filtration through 2 or 3 millimeters of aluminum, proved sufficient to bring about complete cure or at least to allay the pain very greatly. Zimmern (*Paris méd.*, Feb. 7, 1920).

Good results from the **X-rays** in trigeminal neuralgia and sciatica. Matoni (*Med. Klin.*, June 29, 1924).

The measures described under the preceding heading are as applicable in the present form, but in severe cases more active interference is necessary: injections of 70 to 95 per cent. **alcohol**. This method is not safely applicable, however, to the ophthalmic division.

Wilfred Harris has recommended the use of $\frac{1}{8}$ grain (0.02 Gm.) of **morphine** and $\frac{1}{150}$ grain (0.0004 Gm.) of **hyoscine**, hypodermically, twenty minutes before the injection of **alcohol**. This dulls the sensation so as to prevent serious discomfort to the patient, while still enabling the operator to determine, by questioning, when he has penetrated the nerve.

To be entirely effective, the **alcohol** must be injected directly into the nerve-trunk and reach each individual fasciculus. In injecting the maxillary and mandibular divisions, the writer uses a **zygometer**. With the button of this instrument in the auditory meatus, and the inferior edge of the anterior end of the lower bar on a level with the masseteric border of the malar bone, the injection of the mandibular division is made through a point opposite the 2 cm. mark on the lower bar of the zygometer, the needle passing just below the zygoma and making an angle with the skin of 110° from above downward in the vertical plane and 90° from before backward in the horizontal plane. The nerve should be reached between 4.5 and 5 cm. from the surface. For the maxillary division, a point opposite the 3 cm. mark is used, and the needle passes below the zygoma upward and slightly forward, forming an angle of 100° in the horizontal and of 115° in the vertical plane. The nerve should be reached at 5 to 5.5 cm. from the surface. The skin is infiltrated with **procaine**, and once the nerve is pierced (as shown by the referred pain) **procaine** may be injected into it or the

patient lightly anesthetized with gas-oxygen before the 95 per cent. alcohol (not over 0.75 c.c.—12 minims) is injected. No injection should be considered successful unless the peripheral anesthesia resulting is absolute. F. C. Grant (*Jour. Amer. Med. Assoc.*, June 10, 1922).

One hundred cases of trigeminal neuralgia receiving alcohol injections. The author injects the whole Gasserian ganglion in severe cases. Where this procedure was possible, a per-

The possible bad scar about the face is avoided. A deep injection cannot, however, be performed on the supra-orbital nerve. Alcohol may easily be injected into the supraorbital foramen almost by sense of touch. Peripheral avulsion after operative exposure of the nerve is, however, the procedure of choice in supraorbital neuralgia; the scar lies in the eyebrow and is invisible.

In 51 cases, 77 injections were performed, comprising: First division, 5



Injecting third division of fifth nerve from 2-centimeter mark: Method of measuring angle (110°) in vertical plane with protractor. (GRANT, in *Jour. Amer. Med. Assoc.*)

manent cure resulted. When the injection was only partial—especially with preservation of the sensibility of the cornea—recurrence was the rule in from 6 months to 4 years. Some of the patients were cured by reinjection. Härtel (*Münch. med. Woch.*, Aug. 8, 1924).

Injection of alcohol into or avulsion of the infraorbital and inferior dental nerves has been replaced by direct injection of the 2d or 3d divisions at a point as close as possible to their exit from the base of the skull (foramen rotundum and foramen ovale, respectively). The deep injections, when successful, are more permanent in effect than peripheral injection or avulsion.

times, all successful; 2d division, 37 times, 65 per cent. successful; 3d division, 35 times, 84.6 per cent. successful. There were no significant complications. Relief after a 1st injection averaged 14 months; after a 2d injection, 8½ months, and after a 3d, 5 months. F. C. Grant (*Med. Jour. and Rec.*, Feb. 18, 1925).

Alcohol injection into the nerve sheath will give immunity from pain for periods averaging 7 months to 1 year, as indicated in the reports of Frazier, Adson, Coughlin, and numerous others. Much longer periods of relief are also noted. The procedure is not free from risk. The literature is full of mishaps. In injecting the 3d

division, the Eustachian tube may be entered. A too deep penetration for the 2d division may perforate the nose or floor of the orbit. Injection of the 1st division entails great danger and is practically discarded, peripheral **avulsion** being the method of choice. But if the risks are known and all precautions taken, the nerves may be injected just after they leave the skull. Gibbon (South. Med. and Surg., Sept., 1925).

Operative treatment procures the most lasting results, especially **removal of the Gasserian ganglion**, or better, the Frazier-Spiller operation of **division of the sensory root**. The mortality from the latter operation has gradually been reduced to less than 1 per cent.

Aside from alcohol injections, the following surgical procedures are now justified: **Avulsion of the supraorbital and supratrochlear nerves**; **avulsion of the lingual nerve** within the mouth, and **section of the posterior sensory root**. The latter operation has reached such perfection that the prolonged, repeated use of injections in refractory cases is inadvisable. Breniser (Va. Med. Mthly., Apr., 1922).

In 100 cases, the writer resorted to **gasserectomy** for trigeminal neuralgia, with a mortality of 11 per cent. He always tried alcohol injections into the peripheral nerves, preceded by **procaine**, before undertaking the operation, but found that repeated injections of alcohol into the ganglion made the operation difficult. F. Krause (Med. Klin., Dec. 9, 1923).

In 23 cases the author resorted to **section of the sensory root**, with complete success. All the patients are alive and well. He describes the operation as follows: The patient sits up in an ordinary dental chair. **Procaine**, 0.5 per cent., with **adrenalin**, gtt. iij to the ounce, is injected, and the incision is a straight line from the zygoma up just in front of the ear for about 3 inches. The temporal fascia is incised; the lower edge of the temporal muscle

is raised up and pushed forward, and with it the periosteum covering the lower part of the squama temporalis. A hole is drilled here and enlarged downward to the base and laterally until it is almost 3 cm. in diameter. The dura is pushed up, and one works in until he reaches the middle meningeal artery. This is either tied or its foramen plugged, and it is cut. The 3d division is then encountered: the dura covering it is incised and pushed up, and the ganglion comes into view. Working backward, upward and inward, the dura propria is cut, there is a slight gush of cerebrospinal fluid, and the sensory root as it joins the ganglion is plainly exposed. The fibers where they join the ganglion are then cut, a few at a time, beginning with those highest up. The motor root can be identified; it passes behind the ganglion and joins the 3d division in the foramen ovale. It is not cut. Hemostasis is made complete and the wound closed without drainage. W. T. Coughlin (Ann. of Clin. Med., Aug., 1924).

Some patients, after the operation, are annoyed by the inevitable numbness of the face, which feels "wooden," "thick," or "crawly." Most of them very soon grow accustomed to this. Trouble with the eye is avoided by the following simple precautions: (1) Having the anesthetist keep it covered so that no ether fumes reach the cornea; (2) covering the eye at the end of the operation so that the patient cannot touch his anesthetic eyeball; (3) instructing the patient how to wash his eye with salt solution in an eyecup to remove irritating material that he cannot feel because of the corneal anesthesia. E. Sachs (Ill. Med. Jour., Feb., 1924).

The first of Frazier's improvements of the technique of sensory root avulsion was the preservation of the motor root, thus avoiding a bad cosmetic effect from atrophy of the temporal muscle. The second, more recent, improvement bears on the incidence of corneal complications. Where the pain has been referred to the 2d and 3d divisions only, he leaves the inner

and upper fasciculus of the sensory root intact, as this sends fibers to the 1st division which nourishes the cornea. Thus the nerve-supply of the cornea is not wholly ablated and trophic keratitis is prevented. While it is not always possible to carry out these 2 steps, an attempt is made to do so. The motor root, which apparently is devoid of all sensory fibers, is identified with certainty by stimulation with an electrode. General anesthesia is used. F. C. Grant (Med. Jour. and Rec., Feb. 18, 1925).

In none of 25 cases treated by subtotal section of the sensory root was there recurrence of neuralgia after 10 years. Two patients developed trivial corneal lesions while still in the hospital, in both instances yielding promptly to treatment. No case developed corneal complications after discharge from the hospital. C. H. Frazier (Arch. of Neurol. and Psych., Mar., 1925).

Extraction of the posterior root performed in 71 cases without a death. The vast majority of patients are satisfied and tremendously pleased with the relief obtained. A few find the numbness or paresthesia annoying, but this is so rare that the writer has no hesitation in recommending this operation for major trigeminal neuralgia. E. Sachs (Mo. State Med. Assoc. Jour., Feb., 1926).

Sphenopalatine Ganglion Neuralgia.—Sluder has described a neuralgic syndrome or neurosis related to the sphenopalatine (nasal or Meckel's) ganglion. The neuralgia is characterized by severe pain in and about the eyes, radiating to the temple, behind the ear and frequently into the neck, and occasionally to the occiput and tonsillar region. From a point 5 cm. behind the mastoid, where it is apt to be particularly marked, the pain may extend by way of the occiput down to the shoulder. Sometimes the pain is referred to the teeth—a fact which has led to numerous unnecessary extractions. There may be complaint of itching of the soft palate, aching in the throat, a queer feeling in the teeth, metallic taste, and at times scintillating scotoma or a stuffy feeling in the ear.

There is also recognized a sympathetic type attended with a syndrome which comprises sudden severe sneezing, with lachrymation and watery nasal discharge, accompanying the neuralgic pain. The nasal membrane becomes swollen and breathing difficult. The eyes are usually red and injected, and the pupils dilated. The attacks sometimes last a week.

Both the neuralgic and sympathetic types may become chronic, with associated migraine of the "lower half" variety or chronic vasomotor rhinitis and asthma.

A positive diagnosis is reached with difficulty unless the case is seen during an attack and relief obtained upon application of cocaine to the region of the sphenopalatine ganglion. Neurotics and feigners are readily ruled out by an application of sterile water in place of cocaine (Braswell).

Treatment.—If the lesion producing the syndrome is in the ganglion, application of cocaine to the ganglion will give relief. The cocaine may be followed by 2 per cent. silver nitrate solution in mild cases. **Argyrol tampons** in the nasal slit are asserted to control the sympathetic syndrome. The more severe and chronic forms are due to irritation of the ganglion or the postganglionic nerves by infected and hyperplastic sphenoid and postethmoid cells, which will produce the "lower half" headaches, vasomotor rhinitis, and asthma. In these cases radical operation on the posterior ethmoidal and sphenoidal area is indicated (Uren).

Alcohol injection of the sphenopalatine ganglion is favored by Braswell. The posterior end of the middle turbinate is first anesthetized by application of 20 per cent. cocaine solution, then a sword needle about 5 inches long is introduced from the septal side of the nose and, passing through the anesthetized end of the turbinate, is pushed upward, outward and backward through the bony wall which forms the anterior boundary of the sphenomaxillary fossa. Alcohol or 2 per cent. phenol in alcohol, 5 to 15 minims (0.3 to 0.9 c.c.), is now injected. The ganglion may be penetrated by the needle, a sharp pain resulting, but in the majority of cases is only bathed by the solution. The resulting pain lasts from a few minutes to 24 hours. Where the ganglion is penetrated or thoroughly bathed, one injection suffices.

The writer's initial treatment consists of application of 20 per cent. **cocaine** solution to the region of the ganglion on the affected side; 3 to 5 applications are made, followed by a 10 per cent. solution of **silver nitrate**. If pain recurs, the treatment is repeated. If sufficiently long intervals of relief do not result, he then injects the ganglion through the sphenopalatine foramen, going in through the mouth opposite the second molar, about 5 mm. toward the median line of the hard palate, and using a needle long enough to penetrate about 35 mm. (1½ inches). A small amount of 1 per cent. procaine solution is first used to inject ahead of the needle as it penetrates, then 5 to 10 minims (0.3 to 0.6 c.c.) of 5 per cent. **phenol in alcohol** are injected. The pain and burning is much diminished by the procaine, but some stinging and numbness follows, even persisting to the next day. Proper attention must be given in these cases to the patient's general condition, as to **rest, diet elimination**, etc. L. S. Gaudet (New Orl. Med. and Surg. Jour., Sept., 1924).

Glossopharyngeal Neuralgia.—This is regarded by J. B. Doyle as a definite clinical entity, differing from trifacial neuralgia only in the area of distribution of pain. According to Adson, it is similar to trifacial neuralgia in that the pains are spasmodic, excruciating and lancinating, but they radiate from the pharynx and tonsillar fossa to the ear. The pain is brought on by swallowing or yawning, and lasts for only a few moments; the intermittent periods of pain and ease may continue for a few weeks to several months, but the condition always recurs.

Case of a woman aged 42 with ear trouble and tic douloureux of the glossopharyngeal nerve. She had paroxysmal agonizing pain deep in the right side of the neck behind the ramus of the jaw, radiating downward in the neck and sometimes to the affected right ear. The paroxysms lasted from a few seconds to a minute or two. They recurred every few minutes, and were brought on by talking, as well

as by eating, drinking or even by washing the face. Following a radical operation on the mastoid and middle ear, the patient was immediately freed from the neuralgia, and remained so thereafter, except for a few very fugacious pains. L. A. Miller (Ohio State Med. Jour., Mar., 1926).

Cervico-occipital neuralgia is located in the first four pairs of spinal nerves, posterior branches, and is most often a result of exposure to cold or of disease of the adjacent vertebræ.

Cervicobrachial neuralgia involves the sensory nerve-fibers of the brachial plexus, its common causes being cold, rheumatic disorders, or local injury. The pain is situated in the shoulder, and may extend down the arm along the course of the ulnar nerve. According to Oppenheim, brachial neuralgia is a rare disease, and is frequently only a symptom of an organic or functional disorder of the central nervous system or of genuine neuritis. It most often consists in pain in the arm of the ill-defined character and localization of a pain of psychic or neurasthenic origin, rather than that of a genuine neuralgia.

Typical case emphasizing the value of subcutaneous injections of **oxygen**, used extensively by French, Spanish and Argentine physicians. The case was one of neuralgia of the right arm. The oxygen was injected into the subcutaneous tissues at the root of the arm, massaging afterwards to spread the gas. The pain disappeared the next day and had not returned during the months elapsed. Cetrangolo (Semana médica, June 14, 1917).

In a case of neuralgia of the brachial plexus which resisted hot-air baths, electricity, electric light baths, and analgesic drugs, Thobben injected 20 c.c. (¾ ounce) of 2 per cent. **procaine** solution above the

clavicle. Pain, tenderness and swelling were at once relieved, and two weeks later the patient returned to his work.

Purely as a tentative measure, irrespective of any determinable diagnostic evidence, the writer, in a severe case of neuralgia of the brachial plexus, tried a course of **mercury**. The pains disappeared completely for 2 years. Then slight pains returned, but subsided anew under a 2d course, with **neorsphenamin**, and there had been no recurrence during the 1½ years to date. The man was 33 years old, and probably suffered from inherited syphilis. Valls (*Semana méd.*, Aug. 28, 1924).

In rheumatic cervicobrachial neuralgia all of the nerves of the upper extremity are not affected with like frequency nor with like intensity. The points of tenderness are located, in particular, along the course of the musculospiral and radial nerves (musculospiral groove, posterior aspect of the forearm, and first interosseous space). In the neck the most sensitive point is often the paravertebral region of the first or second dorsal segment. The X-ray sometimes shows osteophytes, ossification of ligaments, or a simple rectilinear appearance of the cervical spine. Roger, Reboul-Lachaux and Rathelot (18th French Med. Congr.; *Paris méd.*, Oct. 9, 1926).

Intercostal neuralgia, involving one or more of the intercostal nerves, is, after facial neuralgia, the most frequent and important form. It is seen more often in women than in men, giving rise, when located in nerves distributed to the mammary glands, to the so-called "mammary neuralgia." The comparatively slight and fugitive pains of pleurodynia unassociated with tender points are to be regarded as neuralgic in character. Herpes zoster is seen with especial frequency in intercostal nerve areas (see **HERPES ZOSTER**, Vol. V).

According to Loeper, gastric dys-

pepsia, pain, oppression in the stomach and retarded evacuation may follow and occur as a complication of typical intercostal neuralgia.

When the trunk is bent over toward the affected side, according to Schepelmann, the pain increases in cases of intercostal neuralgia, while in pleurisy the pain increases when the trunk is bent over to the sound side.

Intercostal neuralgia as a cause of abdominal pain and tenderness is exceedingly common, and failure to recognize it often results in futile operations. It may simulate various intra-abdominal, gynecologic or genitourinary lesions. To differentiate parietal from intra-abdominal tenderness the writer advocates a two-stage bedside test. In the first stage the examiner palpates in the usual manner. That his fingers dip fairly deeply into the abdomen before tenderness is elicited does not prove that the tenderness is intra-abdominal, as is shown by the second stage: Keeping his fingers at the most sensitive area discovered on deep pressure, the examiner has the patient make his abdominal muscles rigid by contracting his diaphragm or by raising and holding his head from the pillow. At this point the examiner first relaxes his finger pressure, then reapplies it; he may also exert a little twisting motion with them. If there is intra-abdominal tenderness only, this second stage will fail to elicit any tenderness when strenuous pressure is applied over tense muscles, while if the case is one of parietal tenderness, almost or quite as much tenderness will be elicited by the second stage as by the first.

Excluding peritonitis the author has found tenderness in the parietes more often than in the abdomen itself. Without peritonitis, the great majority of intra-abdominal lesions are free from demonstrable tenderness. Tenderness due to intercostal neuralgia can be demonstrated by deep pressure; by the pinch test; by superficial skin tests, as by pricking with a pin or

applying heat and cold; by pressure on nerve trunks; by pinching flank muscles; by pressure over transverse processes of vertebrae, and by pressure over remote areas, as over the arm when the 1st and 2d intercostal nerves are affected. As a rule, the area of abdominal tenderness in intercostal neuralgia is too widespread to be accounted for by a lesion of a single viscus in the absence of a complicating peritonitis. J. B. Carnett (Surg., Gyn. and Obst., May, 1926).

The treatment of the intercostal form of neuralgias, as of the two preceding varieties, is that of neuralgia in general. Especially good results are obtained from **counterirritation**, preferably the **actual cautery**.

Lumbar neuralgia, involving the branches of the lumbar plexus, presents few symptoms not seen in other forms of neuralgia. The condition of "irritable testis," with pain and syncope attacks, is probably based upon a neuralgia of the nerves of the part.

Coccygodynia is a neuralgia of the coccygeal plexus, most frequent, obstinate, and intractable in women, and often calling for surgical interference.

In the treatment of this condition, Ely has found **manipulation** very successful: The coccyx is grasped between the forefinger in the vagina and the thumb on the outside and is moved backward and forward. The soft parts are also moved about on the bone. The manipulation is begun very lightly and gradually increased in force as the patient becomes less sensitive. Usually 2 or 3 treatments at intervals of 2 or 3 days suffice.

Epidural injections of **lipiodol** found useful. The amount injected was 5 to 10 c.c. (80 to 160 minims), previously slightly warmed. Preliminary local anesthesia with **procaine** is employed, and the injection made with the patient in the knee-elbow posture. A test for proper entrance of the needle

into the epidural space is to inject 2 or 3 c.c. of air, which should disappear, but with the needle improperly placed will give rise to crepitation palpable in the subcutaneous tissues. After the injection the patient is placed in the Trendelenburg position for 4 to 6 hours. Of 5 cases of coccygodynia 2 were cured and 2 improved. Sicard and Coste (Bull. Soc. méd. des hôp. de Paris, Mar. 6, 1924).

Rest and hygiene are indicated until the acute symptoms subside. The **bowels** should be **kept open**. A **hot rectal douche** at 105° F. for 5 minutes twice a day is sedative and relaxing. **External heat** with the therapeutic lamp, 1 hour night and morning, is also of much value. **Faradism**, 1 pole over the coccyx and the other above the sacrum or within the rectum, according to the location of painful spots, is good. The **injection of alcohol** into and about the sensory nerves is often satisfactory. The index finger is retained in the rectum as a guide, a 2-inch needle is introduced through the skin in the posterior raphe and carried to the most sensitive area, and 10 to 20 minims (0.6 to 1.25 c.c.) of 80 per cent. alcohol is slowly injected. The injections may be repeated in 5 to 7 days. They may be given without anesthesia, but most careful asepsis must be observed. If the suffering continues after a thorough trial of palliative treatment, **excision of the coccyx** is required. C. J. Drueck (Western Med. Times, Mar., 1920).

Metatarsal neuralgia, or **Morton's disease**, is due to a depression of the arch of the foot, resulting from debility, or excessive body weight for the strength of the foot. It may also be due to too short or too narrow footwear.

Typically, the pain results from jamming of the superficial branch of the external plantar nerve and its 2 digital branches between the heads of the 4th and 5th metatarsal bones, due to lateral pressure against the latter. On walking, pain is felt about the 4th and little toes and the distal por-

tions of the corresponding metatarsals. Squeezing the foot with the hand will induce the pain.

The final remedy in difficult cases lies in the **excision of the branches of the plantar nerve** which are affected by the pressure. This may be effected by opening over each of these branches; but a single incision can sometimes be used for 2 branches. The nerves should be attacked at a point beneath the proximal extremities of the metatarsal bones. Van Hook (Ill. Med. Jour., July, 1913).

Metatarsalgia being a symptom associated with some deformity of the transverse arch, in an early case an attempt must be made to restore the lost muscle power by **massage, exercise, faradic stimulation, and suitable shoes**. The latter must be of the full width of the foot when bearing the body weight, and the soles absolutely flat from side to side. If there is pain on lateral compression, firm **strapping** with rubber plaster around the waist of the foot will usually give relief. In late cases some form of **anterior arch support** may become necessary. G. P. Mills (Pract., May, 1922).

In foot pain due to depressed anterior metatarsal arch, a **leather lift** is fastened to the sole of the shoe at and behind a line joining the heads of 1st and 5th metatarsals. The lift is merely a triangular wedge which prolongs the sole backward and shortens the shank. Only the heel and apex of the lift touch the ground, the toe being about $\frac{1}{4}$ inch higher. The amount of lift depends largely on the comfort of the patient. The metatarsal arch is elevated by this device, allowing the toes to drop. Good results were obtained in 30 cases. The lift may be used not only for metatarsalgia, but also for callus under the anterior arch, fracture of the toe, paralytic feet with dorsally flexed toes, and following operations for hallux valgus. B. H. Kyle (Va. Med. Mthly., Aug., 1925).

Neuralgia of the heel consists of pain and tenderness in this location which resist ordinary measures.

Painful heel, according to Steinhardt, is often due to acute inflammation of the os calcis, and there is frequently a history of gonorrhea, gouty rheumatism, or trauma. The X-ray will show exostosis of the os calcis, with surrounding periostitis. The condition is curable by **removal of the exostosis**, with **postoperative treatment of the underlying cause**.

The commonest form of painful heel is the "bruised heel," the treatment of which is **rest in elevation** for 3 days, with bathing of the foot twice daily in **warm water** containing a little **sodium carbonate**. The next commonest cause is true achillobursitis, usually bilateral and easily recognized. The treatment is **rest** without boot or shoe for 3 days; gentle **massage** for 15 minutes twice daily with an **iodine salve** with **methyl salicylate**, and the use of shoes with an ample posterior bow to the heel. Some cases are immediately relieved by **raising the heel** $\frac{1}{2}$ inch. Another cause of sudden acute pain is true tenosynovitis of the tendo Achillis. The treatment is **compound mercuric ointment** and a simple **back splint** fitted with a rigid **right-angled foot-piece**, together with rest for 1 week. Other possible causes include tuberculous osteomyelitis of the os calcis, a gonococcal inflammation of the plantar fascia, calcaneal spur, chilblains in the heel, and tabes dorsalis. Stiell (Pract., May, 1922).

Neuralgias of the nerves of the legs, described as crural, plantar, etc., present the usual features of neuralgia in general and need not here be elaborated.

Neuralgia of the rectum is a distressing form which fortunately readily responds to appropriate internal and local treatment.

The writers review the methods of treatment applied in neuralgia of the rectum by Loomis (**chloral, bromides, acetphenetidin, cocaine suppositories, and morphine**); Gant (applications of **camphor, capsicum, and chloroform**); Davis (**belladonna**); Ein-

horn and Gant (**electrotherapy**); Albu (**dilatation and elongation of the nerves**); but have found that brief **tepid douches followed by hot douches**, of 3 minutes' duration, are very beneficial. Parmentier and Foucaud (*Presse méd.*, July 6, 1910).

Case of typical primary neuralgia of the rectum in a boy 18 years of age. The only treatment that gave permanent relief was **warm sitz baths**. Dritsaki (*Roussky Vrach*, Aug. 18, 1912).

CAUSALGIA.

Causalgia, or *thermalgia*, has been defined as a severe burning pain following injury of a nerve, or, more specifically, as a pain due to an ascending neuritis in a nerve trunk, or involving the peripheral sympathetic. The first syllable of the term, "caus," is derived from the Greek word signifying "a burning;" hence, caus-algia, "a burning pain."

ETIOLOGY.—Marked interest in this condition was aroused during the World War on account of its occasional occurrence in wound cases. Injuries of the median and sciatic nerves and of the brachial artery proved the most troublesome. Leriche formulated the theory that the condition is due to vasomotor disturbances resulting from injury to sympathetic fibers in the perivascular sheath of the wounded artery. The pain, according to this view, is the result of irritation of the perivascular sympathetic plexus on account of pressure exerted by cicatricial tissue. Applying this view in practice, Leriche removed a part of the sheath of the artery in the affected region in a number of cases, with satisfactory results.

As described by Tinel, the pain sets in early after the injury and reaches its height in 2 or 3 weeks. It is severe and persistent, sometimes occurring both by day and by night, and is particularly marked in the hand, even if the injury be situated more proximally. Generally the pain extends to the upper arm. There is pronounced hyperesthesia, but deep pressure is not painful. Heat, cold, tactile contact or motion of the part may bring on pain. Paralysis and sensory impairment are unusual, the condition occurring, as a rule, where lesion

of the nerve is only slight. The skin surface is apt to be thin, white or glossy, though sometimes reddened. Trophic disturbances occasionally coexist, but are not pronounced. According to Lewis and Gatewood, the pain attains its maximum intensity 4 to 6 months after nerve injury and then slowly diminishes.

Aside from traumatic causalgia, Tinel (*Presse méd.*, Apr. 2, 1921) has applied the terms *spontaneous causalgia* and *sympathetic algia* to cases witnessed independently of injury and in which the discomfort is not an actual pain, but rather a sense of burning and pulsation. The nerves oftenest affected are those having walls rich in sympathetic fibers. There is always involved some irritation or compression of the sympathetic centers, inducing in them a condition of erethism which becomes manifest in local neuralgia, with a feeling of tension, numbness, and burning pain, together with vasomotor disturbances. The condition is apt to develop in those predisposed to it by having an irritable sympathetic system. In his cases the hands, thigh, or leg, face and neck or pelvis were the regions affected.

TREATMENT.—In the milder cases, cold, wet compresses, anodal galvanic baths, and ionization may prove serviceable. Spiller has referred to a patient who for 6 years slept every night with her hand in a basin of cold water, pain returning when the water became warm. Boschi and Tanfani reported rather good results from high frequency currents in cases following war wounds. In the type of case described by Tinel, the condition tends to subside under physical and mental rest. He also attempts to find and remove the cause of sympathetic irritation, uses potassium iodide and calcium chloride in cases showing evidence of vascular spasm, and practices psychotherapy to the extent of reassuring the patients that recovery in time is certain with proper rest and hygiene.

In the typical traumatic cases, Lewis found injection of 60 per cent. alcohol into the nerve a very effective measure, the pain often disappearing permanently within 24 hours. In using such an injection the nerve is exposed and 1 or 2 c.c. (16 or 32 minims) of the alcohol injected intraneurally at a point above the injury. Sicard and Dambrin, using 70 per cent. alcohol, were

able to report 27 cures out of 32 cases as the late results.

In severe cases the condition is so troublesome that, some decades ago, even amputation of the limb was resorted to. Later, nerve resections were performed. Leriche's **periarterial sympathectomy** consists in exposing the arterial trunk and removing the connective tissue around it for a distance of several centimeters with fine scalpel and forceps. Turbin moistens the artery as a test. If any connective tissue remains, the vessel is flesh-colored; if not, it is gray. This author did 8 such operations, comprising 5 on the brachial artery and 3 on the femoral or popliteal. Prolonged conservative treatment and neurolysis had failed, but Leriche's operation was followed by rapid improvement. Pain and contractions disappeared, the trophic, vasomotor, and secretory disturbances decreased, and motility of the limb was restored. Platon reported 18 war cases in which the pain was entirely allayed after the operation, ceasing at once in 16 and more gradually in the other 2.

Having performed 25 operations in these cases the writer concluded that the efficacy of early **resection** and **suture** for severe causalgia is beyond criticism. H. Platt (*Brit. Med. Jour.*, Apr. 23, 1921).

The proper treatment for major causalgia is **excision** of the affected portion of nerve, followed by end-to-end **suture**, if possible, or by **nerve-graft** where apposition of the divided ends cannot be obtained. H. S. Carter, Jr. (*Jour. of Neurol. and Psych.*, May, 1922).

MIGRAINE.

DEFINITION.—A form of severe paroxysmal headache often accompanied by nausea and vomiting. Called also "hemicrania," "neuralgic headache," "sick headache," etc.

SYMPTOMS.—Premonitory symptoms extending over a few hours to a day or two are not uncommon, these being mental hebetude, somnolence, or despondency, with vague uneasiness or ill-defined discomfort. There

may be an abnormal hunger on the preceding day. Abnormal visual phenomena are also frequently seen prior to onset of the attack, these consisting of visual hallucinations, such as dark spots or bright lights of angular shape; pupillary abnormalities, hemianopsia, and indistinctness of sight. Disturbances of other sense mechanisms are more rare, although sometimes shown, such as anesthetic areas about the head and face, tingling followed by numbness, aphasia, and transient mental disorder or confusion of ideas. Following these prodromal symptoms more or less closely, or accompanying them in quickly developing cases, we have the characteristic headache, generally starting in the morning, at first unilateral, located in the temple, eye, or occiput, but spreading as it increases in intensity until it involves all of one side of the head, or in some cases both sides. The pain is intense, throbbing, and is increased by movement, noises, light, and any worry or emotional strain. Nausea is usual and vomiting frequent, becoming, in the so-called bilious headache, very distressing. This vomiting in occasional cases gives relief, its occurrence marking the end of the attack; but the usual rule is that the pain is increased and rendered more unbearable by the vomiting. The face is sometimes flushed, sometimes pale; the pulse is slow and the arteries throb and have a sclerotic feel to the touch. There is great prostration and physical weakness, and complete loss of appetite. Temperature abnormalities are sometimes present, but are neither constant nor characteristic. The urine is sometimes abundant, sometimes almost suppressed. Constipa-

tion at the beginning of the attack is the rule. The patient is disturbed by noise and light, and prefers to remain alone in a darkened room.

The duration of the paroxysm is variable, from a few hours to several days. Twenty-four to thirty-six hours of suffering are frequent, and in the severer forms the patient may be kept in bed three or four days. The attacks recur for years, or, in rare cases, through life. In old age they usually cease, and in many women there is complete cessation after the climacteric. The seizures in women are apt to occur at or near the menstrual periods, although periodicity may be noticeable independently of this. They may occur as often as 2 or 3 times a week.

The attacks subside slowly, as a rule. With the beginning diminution of the pain the patient falls asleep, and awakes some hours later free from the pain and often feeling better than before the attack.

In some instances manifestations of sympathetic disturbance are noticeable, *e.g.*, dilatation of the pupils with contraction of the temporal artery or *vice versa*; pallor or flushing; lacrymation; sinking in of the eye on the affected side; unilateral hyperidrosis, and coldness and sweating of the hands and feet.

In unusual cases the pain may be replaced by nausea, vomiting or vertigo. Vomiting occurs especially in persons subjected to eye-strain.

The term *ophthalmic migraine* is sometimes applied to the common form in which the ophthalmic division of the 5th nerve is involved, with visual hallucinations, hemianopsia, scotoma, and dimness or temporary loss of visual power.

In *ophthalmoplegic migraine* the attacks eventually are attended with paralysis of one or more ocular nerves on the affected side, more frequently the 5th than the 4th or 6th nerve, and are apt to be prolonged, lasting 2 or 3 days instead of the more usual 1 day. The paralysis may become permanent. In this variety the pain is regularly unilateral, although it may pass from one side to the other in successive attacks. It is generally located in the temple, whereas in other varieties it may be situated in the frontal or parietal region, behind the ear or in the occiput.

In a woman of 60 years, attacks of migraine were accompanied by albuminuria and high blood-pressure. During the intervals the urine, blood-pressure and blood urea were normal. San guinetti (Policlin., Mar. 16, 1925).

DIAGNOSIS.—The diagnosis of migraine is without especial difficulty, the presence of the characteristic headache and other clinical symptoms above mentioned being all-sufficient. It is to be remembered that neuralgia and other forms of headache may occur in a patient who suffers from migraine, and likewise, that migraine is not necessarily unilateral, except in the ophthalmoplegic cases.

The diagnosis of migraine is based by Clarke on the following points: (1) Marked hereditary tendency, direct transmission, and absence of other neuroses in the family. (2) Onset usually in childhood. (3) Visual phenomena preceding the headache, especially temporary hemiopia. (4) Headache generally unilateral. (5) Vomiting generally accompanying the onset of headache and ushering in improvement. (6) Return to normal in the intervals. (7) Temporary loss of speech and sensory disturbance in some severe attacks.

ETIOLOGY AND PATHOLOGY.—Regarding the pathology of

the affection there are some differences of opinion. There are no discoverable anatomical lesions in simple migraine. Dejerine regarded ophthalmoplegic migraine as being usually the result either of a basal tumor or of basal syphilitic or tuberculous exudates. Various basal tumors have actually been found in autopsies in this type of case.

One of the theories of the origin of migraine is that of Liveing: That the affection is a neurosis in which there occur periodical sensory discharges analogous to the motor discharges of epilepsy. Modern investigations, however, have traced both the latter disease and migraine in many instances to endogenous toxics, probably intermediate waste products derived from foodstuffs.

The frequent interchange of epilepsy and migraine in different generations of the same family clearly indicates a definite relation between the two diseases. In cases seen by the writer there occurred substitution of one neurosis for the other in the same individual. Symptoms of epilepsy in an attack of migraine may, however, indicate the existence of a relationship between the two diseases in that attack, and need not, according to the dictum of Moebius, stamp that attack as epileptic. Waterman (Boston Med. and Surg. Jour., Mar. 5, 1914).

By others migraine is regarded as a neuralgic affection of the ophthalmic division of the fifth nerve. By others still it is looked upon as a "vasomotor neurosis." Indeed, the most widely accredited view at the present time is that the attacks are due to a localized vasomotor spasm of cortical vessels, while the pain is of peripheral nerve origin.

From study of the urine and blood in 48 cases, the writers look upon mi-

graine as the result of combined hepatic and renal inadequacy. It is the expression of a gradually increasing intoxication, causing euphoria at first, later pain and defensive manifestations such as anorexia and vomiting, and involving particularly the nervous system, including the sympathetic and vasomotor structures. Rémond and Rouzaud (Bull. de l'Acad. de méd., Dec. 28, 1920).

In three cases reported by Renner, periodically recurring migraine was accompanied by hemiplegic manifestations, which would vanish along with the other migraine symptoms.

Ophthalmic disorders prove causative in a comparatively large number of cases through reflex irritation of the ophthalmic division of the fifth pair. Numerous instances exhibiting the influence of eye-strain in migraine have been recorded. The factors most emphasized are astigmatism, excessive accommodative effort, and strain of the extraocular muscles in attempts to secure binocular vision. Hypertrophy of the turbinates may act similarly. Gastrointestinal disorders seem frequently to bear an etiologic relationship.

According to Hunt, the condition is a periodic angiospasm or angio-paralysis of cerebral vessels due to an autotoxic influence on the sympathetic and vascular systems. Some have compared it to an anaphylactic reaction. Others have invoked thyroid disturbance or periodic swelling of the pituitary body. A relationship to inherited or acquired syphilis has at times been suspected.

Case of ophthalmoplegic migraine which occurred only after parturition, appearing after each child-birth and subsiding within a few weeks. The external rectus of the right side was the muscle chiefly involved, in-

stead of the usual oculomotor paralysis; the case was peculiar also in the occurrence of multiple recurrent styas. The conditions point to a toxemia as the exciting cause. A. Brav (Jour. Amer. Med. Assoc., Mar. 14, 1914).

Protein hypersensitivity is the cause of much migraine, and skin tests were successfully applied by the writer. Both migraine and epilepsy disappeared when the offending substance was removed from the diet. M. Craig, Wallis and Nicol (Lancet, Apr. 14, 1923).

Hereditary predisposition is the most frequent and important etiological factor. Women of neurotic families are the greatest sufferers from the disease, although the affection is by no means uncommon in men.

Families of 127 cases studied as to heredity.

In 100 families, either the father or the mother had migraine, with 143 migrainous children and 488 non-migrainous children, or a ratio of 3.13 to 1.

Among 7 families in which the parents were migrainous, 10 children had epilepsy alone or a migraine-epilepsy syndrome; 37 children had neither epilepsy nor migraine, a ratio of 3.7 to 1.

Seven families were tabulated as crossing of persons with dormant migraine; the migraine in these was not present in the father or the mother of the family, but was present in the brother, sister, father or mother of the parents of the families studied. In this group, 30 children had migraine and 85 did not have migraine, a ratio of 2.83 to 1.

Three families were studied in which the presence of migraine in both parents was carefully investigated. All of the 15 children of this group had migraine.

The total number of children studied was 198 with migraine and 610 without, a ratio of 3.08 to 1.

The results of this study definitely establish the hereditary nature of the affection. Buchanan (Med. Rec., Nov. 13, 1920).

Migraine is transmitted in heredity as a dominant in the Mendelian sense. Often these cases show some degree of psychic instability. Infectious diseases, in particular influenza and encephalitis, seem to favor the appearance of migraine. The same is true of trauma, but such cases are nearly always of severe grade, with epileptoid manifestations, a tendency to progression, and interparoxysmal periods not entirely free of trouble. The typical ophthalmic migraine arises from a variety of occasional causes, and is often preceded by prodromes, such as asthenia and prostration, or excitement and irritability, sensitiveness to noises or odors, and digestive, vasomotor or secretory disturbances. These prodromes, generally, assume a definite type in each patient. Among atypical forms of migraine are the hemicrania cerebellaris of Oppenheim, featured by vertigo, and the purely hemianopsic form. Cases in which pain is followed by aphasia, apraxia or ptosis are exceptional, and are possibly not true migraine. Ophthalmoplegic migraine cannot be considered a true migraine, as it shows a progressive course ending in permanent paralysis; it is always an evidence of a gross lesion—meningitis or tumor. Migraine in children often ceases at puberty. V. Christiansen (Paris méd., July 18, 1925).

It is more common among the educated upper classes than among the laboring class. It generally makes its first appearance at or near puberty; rarely, if ever, after middle life. Sometimes it begins in early childhood. Overwork at school or in business, worry, lack of open-air exercise, wasting and diathetic diseases predispose to the affection, and reflex causes are often traceable, especially disorders of the female generative organs and

refractive errors and ocular muscular insufficiencies. The exciting causes immediately preceding the paroxysm are manifold and various, it being also remembered that even when there is no exciting cause the rhythmical recurrence of the seizures will not be broken. As a rule, when the usual time between attacks has nearly or quite passed, any suddenly produced nervous impression will precipitate the attack.

The common exciting causes are: Indiscretions in eating, excitement, fatigue, emotional outbursts (anger, grief, etc.), loud disturbing noises, visual impressions of moving objects (as of railway trains, passing crowds, a rapidly moving field in microscopical work, riding backward), etc. Toothache from carious teeth and the presence in children of adenoid growths in the nasopharynx act also as immediate causes.

Migraine should be carefully distinguished from the headaches due to the eyes or accessory sinuses. It is an angiospasm of the brain dependent upon an attack of sympathetic irritation. Angiospasm of the vascular area of the ophthalmic division and dura accounts, for simple migraine; angiospasm of the cortico-calcarine region, for ophthalmic migraine, and of the Rolandic region, for migraine with paresis, aphasia and numbness of the hands and face. These conclusions are supported, among other reasons, by the induction of attacks by immersion of the hands in cold water or by application of ice to the forehead, and by the relief obtained from pressure on the carotid (with its pericarotid plexus), amyl nitrite, and cervical sympathectomy. As for the factors which excite the sympathetic to induce migraine, anaphylaxis accounts for some cases—those associated with urticaria, angioneurotic edema, asthma, hay fever, eczema, paroxysmal tachycardia, cyclic

vomiting, ingestion of certain foods (as chocolate, eggs, milk, meat, beans) or the inhalation of odors. In such cases ingestion of 0.5 Gm. ($7\frac{1}{2}$ grains) of peptone 1 hour before meals may give relief. A second fairly distinct group is that of migraine of endocrin origin, comprising the menstrual type, a type connected with insufficient menstruation or castration, and the types connected with hypo- or, more rarely, hyperthyroidia. Of the migraines of digestive origin, some are doubtless dependent on colloidoclastic shock and favored either by insufficient proteo-pexic function of the liver or by anaphylaxis to certain foods or drugs. Among the migraines of reflex origin are those due to gastroptosis, duodenal stenosis, gall-bladder stasis (improved by non-surgical drainage), and appendicitis. Causes which sometimes act reflexly are utero-adnexal lesions, refractive errors, ocular or nasal lesions, and sinusitis. A fifth group of exciting causes comprises cold, heat, climatic variations, emotions, and fatigue. Pasteur Vallery-Radot (Paris méd., July 18, 1925).

PROGNOSIS.—Even frequent recurrence of migraine seems to have little unfavorable effect upon the general health, and life is not endangered nor probably shortened by the affection, although a few cases have developed fatal thrombosis of cerebral vessels. The disease, as above said, often spontaneously subsides after middle life. It may disappear for years, then recur. Many cases are improved by treatment, in that the attacks are diminished in number and in severity, and the individual paroxysms may be aborted or quickly relieved.

A complete cure—*i.e.*, to the extent of entirely preventing recurrence of the headaches—is, however, seldom obtained. The outlook is more favorable where there is obvious, but removable impairment of health or

some removable source of reflex irritation, such as eye-strain. The most unfavorable and intractable cases are those in which strong hereditary predisposition exists.

In ophthalmic migraine permanent ophthalmoplegia, hemianopsia, amaurosis, aphasia or hemiplegia occasionally results.

TREATMENT.—When, as is often the case, the patient is aware of the causes which produce the paroxysms, the first requisite is a rigid avoidance of these causes. In children the first attack of hemicrania should suggest a careful search for ocular insufficiencies or other possible reflex cause, and in all children of neurotic families having a predisposition to migraine especial hygienic precautions, as to avoidance of eating excessively, long hours of study, etc., should be observed.

Mitchell advocated the following measures for the prevention of migraine: **Diet:** Red meats to be excluded; fish, bacon, brains, sweet-breads, and eggs allowed. Rich, highly spiced dishes, coffee, tea, and alcoholic beverages to be excluded. Sweets to be reduced. Water may be taken very freely. Meals at regular intervals. Plenty of outdoor exercise, avoiding undue fatigue. Rooms to be well ventilated by day and night. Hot baths 2 or 3 times a week. In some cases the Turkish bath is beneficial; in others, the morning cold sponge bath. Salicylates are useful. In obstinate cases an occasional mercurial is required. Best results from long-continued use of Rachford's formula:—

R. Sodium sulphate

(crystals) gr. cxx (8 Gm.).

Sodium phosphate ... gr. xxx (2 Gm.).

Sodium salicylate .. gr. x (0.6 Gm.).

Tincture of nux

vomica gtt. iij.

Distilled water,

to make fʒiv (120 c.c.).

This dose to be taken before breakfast, each morning, preferably in a glass of Seltzer.

Migraine sometimes occurs in children after they have outgrown a tendency to cyclic vomiting. In the nervous children with migraine, country life, brief hot or cold douches, and potassium bromide night and morning are useful. The disorder may in some cases prove to be due to anaphylaxis to some food, such as eggs or chocolate. Comby (Arch. de méd. des enf., Jan., 1921).

Migraine may be due to gall-bladder distention the result of bile-duct obstruction. Sensory innervation of the gall-bladder being exclusively sympathetic, the disturbance becomes operative by this route. The migraine may be further promoted by infection in the stagnant bile. Non-surgical biliary drainage overcomes this condition. Permanent recovery usually follows from 1 to 6 such treatments, though in some the intubation has to be repeated every 1 to 3 months. M. Chiray and F. Triboulet (Presse méd., Mar. 11, 1925).

Antisymphilitic treatment may cure ophthalmic migraine with scotoma. In this event a latent syphilitic arteritis may be considered as having been the cause of the condition. Pinard (Médecine, Nov., 1925).

When an attack supervenes the first requisite is absolute mental and physical rest and quiet, and this in mild cases may be sufficient to give relief within an hour or two. Usually other remedies are required.

Calcium lactate used with success.

At the first sign of an attack, 30 grains (2 Gm.) must be taken immediately. It should be constantly carried by sufferers, and for this purpose the tablet form is essential. The tablets must be fresh. It does not cure migraine, but aborts the attack. Bigland (Brit. Med. Jour., Dec. 15, 1923).

Among the most valuable drugs are the coal-tar derivatives, singly or in combination, and caffeine, sodium salicylate, acetylsalicylic acid, guarana, ammonium chloride, bromides, chloral, cannabis, and a long list of

similar drugs. **Antipyrin** is sometimes quite effective. **Acetanilide** has also been recommended. A brisk **purge** may give definite relief.

According to Herzfeld, **quinine** is of excellent service during the early stages, during the time of the gastrointestinal disturbance, as well as during the stage of scotoma. The usual dose is 7 grains (0.46 Gm.); rarely, a second dose is required.

During the attack of ophthalmic migraine gentle and slow **massage** should be practised **around the orbits**, with especial pressure over the temporal arteries, or a weak **galvanic current** may be applied. The following cachets should be taken every half-hour up to the limit of safe dosage:—

℞ *Antipyrina* gr. viiiss (0.5 Gm.).
Acetphenetidini . gr. iij (0.2 Gm.).
Acetanilidi gr. iss (0.1 Gm.).
Caffeina gr. ¼ (0.05 Gm.).

M. et ft. in cachetam no. j.

If antipyrin has already been found inefficient, 15 to 30 grains (1 to 2 Gm.) of **potassium bromide** should be given instead, or **cannabis** may be employed:

℞ *Ext. cannabis*.... gr. ¼ (0.016 Gm.).
Acetphenetidini,
Acetanilidi ..ãã gr. iiss (0.16 Gm.).

M. et ft. in pilulam no. j.

In the intervals between attacks an important requirement is to **correct** any ophthalmic disorder, especially **errors of refraction**. To exert a sedative effect, appropriate **hydrotherapy** and **bromides** are indicated. The first should consist of **interrupted jets of lukewarm** (32° C.) **water** to the entire **body**, except the head and neck, for 2 or 3 minutes, followed by a brief application of **cold water to the feet**. The bromide may be prescribed thus:—

℞ *Potassii bromidi* .. 3iiss (10 Gm.).
Sodii bromidi,
Ammonii bromidi,
Sodii benzoatis, ãã gr. lxxv (5 Gm.).
Syrupi aurantii .. f3ij (60 c.c.).
Aqua destillata,
q.s. ad f3x (300 c.c.).

M. Sig.: One tablespoonful before dinner and supper.

Gastrointestinal disturbances play an important part in the etiology. To correct these conditions **exercise** in moderation and life in the **open air** will be of assistance. **Mental fatigue** and the use of **tobacco** are to be **interdicted**. In the diet restriction of meats is especially to be insisted upon. **Stimulating beverages** of all kinds must be **proscribed**.

Each morning a half-tumblerful of an **alkaline solution**, prepared by dissolving the following salts in a quart of water, should be taken on an empty stomach:—

℞ *Sodii sulphatis* ... 3j (4 Gm.).
Sodii bicarbonatis. gr. lxxv (5 Gm.).
Sodii phosphatis . 3iiss (10 Gm.).

M. et pone in chartulam no. j.

Where constipation does not yield to these salts, the following combination may be used:—

℞ *Fluidextracti frangulae*,
Fluidextracti cascaræ sagradae ãã f3vj (25 c.c.).
Glycerini f3x (40 c.c.).

M. Sig.: One teaspoonful in a half-glassful of water before retiring.

R. Oppenheim (N. Y. Med. Jour., from Progrès méd., Sept. 28, 1912).

One of the snuffs recommended by Lorand is formulated as follows:—

℞ *Mentholis* gr. viiiss (0.5 Gm.).
Acidi borici ... gr. xv (1 Gm.).
Radiciis iridis,
Lactosi ãã 3ss (2 Gm.).

M.

Lohman found that an attack could be cut short by **massage of the nape of the neck** precisely at the insertion of the muscles into the occiput, while Andrews recommends **dietetic restrictions**. Andrist (St. Paul Med. Jour., Mar., 1913).

In 2 cases of ophthalmic migraine **benzyl benzoate** proved very effective. In 1 case 30 drops of the 20 per cent. alcoholic solution regularly aborted attacks when used early, and checked them in 20 minutes where scintillating scotoma was already present. In the

other case, 20 drops taken 4 times daily for months markedly reduced the frequency and severity of the attacks. Delorme (*Arch. d'ophth.*, Jan., 1924).

Special attention has been directed to the value of **phenobarbital** (luminal) by Wilfred Harris and others.

Reference to a close relationship between true migraine and epilepsy. Good results obtained with **phenobarbital**, not exceeding $\frac{3}{4}$ grain (0.048 Gm.) 3 times daily at first and later reduced to twice or once daily or even less. Occasionally, larger doses are required. W. Harris (*Brit. Med. Jour.*, Oct. 28, 1922).

Phenobarbital used systematically in 75 definite cases (hereditary taint, hemicrania, nausea, vomiting, and disturbances of vision during the attack). The drug decreases cortical irritability, which is the ultimate cause, and also acts as vasodilator. In 5 cases there was a history of epilepsy in the family, while 12 patients had epileptic symptoms. With hygiene and the dietetic measures indicated for epilepsy, the drug caused considerable improvement in 75 per cent. of cases. In 3 cases with a spasmophilic diathesis, intravenous injections of **calcin** caused decided improvement. The dosage may be lower than in epilepsy, beginning with 0.025 Gm. ($\frac{3}{4}$ grain) 2 to 3 times a day, which may be maintained or decreased if it has a good effect, or increased to 0.05 Gm. ($\frac{3}{4}$ grain) 2 to 3 times daily, but never to more than 0.1 Gm. ($1\frac{1}{2}$ grains) twice a day. Attacks with long prodromal symptoms or typical periodicity may be aborted by 0.05 to 0.08 Gm. ($\frac{3}{4}$ to $1\frac{1}{4}$ grains) 2 to 3 days before the attack. The drug may also yield good results in symptomatic migraine, and in brain syphilis, progressive paralysis, and brain tumor. G. Stiefler (*Deut. Zeit. f. Nerv.*, Jan., 1924).

Where the attack is associated with nasal obstruction, spraying **cocaine** solution in the nose may yield marked betterment.

When other remedies fail, hypodermic injections of **morphine** will usually give prompt relief. Inhalations of **chloroform** may also be resorted to, but are not to be used when other means will suffice.

According to Harris, the cause of the headache in migraine is almost certainly congestive, due to dilatation of the superficial arteries following the initial vasomotor spasm which produces the aura of hemianopsia, color spectrum, tinglings, aphasia, etc. To relieve the actual pain cardiac depressants, such as **chloral hydrate** and the **coal-tar analgesics**, are often successful by lowering blood-pressure, the patient being kept quiet, lying down, with the head as high as possible. Ten grains (0.6 Gm.) of **Dover's powder**, followed by a hot drink containing $\frac{1}{4}$ grain (0.01 Gm.) of **pilocarpine nitrate**, promotes perspiration and may give speedy relief.

Good results from Lauder Brunton's recipe of 15 grains (1 Gm.) of **sodium salicylate** and 30 grains (2 Gm.) of **potassium bromide**, given at the very onset of the attack, and repeated if necessary. The writer is opposed to the use of morphine. A bed in a cool dark room and a cup of strong **black coffee** was the prescription of the late James Stewart. A. H. Gordon (*Internat. Clin.*, 1:120, Ser. 34, 1924).

The danger of the establishment of a drug habit should be constantly borne in mind, and the patient be not permitted to use opium, chloroform, or similar remedies indiscriminately nor on his own responsibility. It is also noteworthy that each case must be treated individually, and that remedy employed which experience shows gives in the particular case most relief with least subsequent harm. What will entirely and quickly cure one patient may produce absolutely no effect upon the next case, and after long use any drug is liable partially to lose its effect.

Clem has used **potassium iodide** in migraine to the exclusion of all other remedies, partly on the basis of the similarity between the headaches of migraine and of cerebral syphilis. In the most aggravated cases the iodide in 5- to 15-grain (0.3 to 1 Gm.) doses, 3 times daily, diminished both the frequency and severity of the attacks.

Review of the history of 1335 cases, 75 per cent. of which had undergone 1 to 7 operations of various kinds. Not a single patient operated on was cured or relieved more than temporarily, while those who had their reproductive organs removed, or a gastro-enterostomy performed, were made much worse. J. A. Buchanan (Surg., Gyn. and Obst., May, 1924).

Report of 8 cases of migraine and 10 of epilepsy indicating that foci of infection may play an important part in these conditions. They can be mitigated in most instances and arrested in some through surgical removal of such foci. Of the 8 migraine cases, cessation occurred in each. Five require **colectomy**; 2 of these were not entirely relieved until after the **removal of dental infection**. Two were relieved chiefly through **removal of infection of the cervix** and 1 through **antrum drainage**. The simplest and safest detoxicant measures should be carried out first. J. W. Draper (Jour. Fla. Med. Assoc., July, 1924).

Léopold-Lévi and de Rothschild maintain that migraine in adults, and especially in children, is sometimes of hypothyroid origin. They report favorable results in children from small doses—usually 5 mgm. ($\frac{1}{12}$ grain)—of **thyroid**. Lévi states that menstrual and anaphylactic forms of migraine also respond to this measure.

Measures other than the administration of medicines also frequently give relief. Among these the **galvanic current** to the temples and back of the neck ranks high, often breaking up an attack, and when used continuously for some weeks diminishing to

a great degree the tendency to migrainous attacks. **Hot or cold applications** to the head may be employed. **Counterirritation** to the head by the **actual cautery**, **mustard plasters**, **menthol**, etc., is frequently helpful, as is also a **hot foot-bath**. **Gastric lavage** has been advised.

During the intervals between the paroxysms **hygienic measures** directed toward the improvement of the general health are indicated. A **change of climate** is often helpful. The long-continued use of **nitroglycerin** and the **bromides** seemingly exerts a favorable influence over the course of the disease. Gowers, to improve vasomotor stability, advocated prolonged, combined use of **nitroglycerin** and **strychnine**.

According to Schottin, migraine is due to poverty of the cortical centers in phosphorus. He, therefore, treats it with a combination of **phosphorus** and **lecithin** in oil, with asserted favorable results.

Complete arrest of migraine reported from 5 to 8 intravenous injections of **sodium carbonate**, each of 1.5 to 2 Gm. (23 to 30 grains), together with 2 or 3 Gm. (30 to 45 grains) of **sodium bicarbonate** daily before meals. Their anticollonoidoclastic properties are the source of benefit. Sicard (Bull. Soc. méd. des hôp. de Paris, July 22, 1921).

Individual migraine cases react differently to various treatments. One may be relieved by a **lactovegetarian diet**, another by **emotional quiet**, others by **regular working hours** or by **hydrotherapy**. In different cases the writer advocates **bromides**, **arsenic**, **phenobarbital**, and especially **nitroglycerin**—3 or 4 drops of the 1 per cent. solution 3 or 4 times a day. The derivatives of **salicylic acid**, **belladonna**, **ergotin**, **aconite** and **cannabis** serve only to subdue attacks. V. Christensen (Paris méd., July 18, 1925).

E. D. BONDURANT,
Mobile.

